POLICY FORUM: EPIDEMIOLOGY

Elimination of Syphilis in the United States

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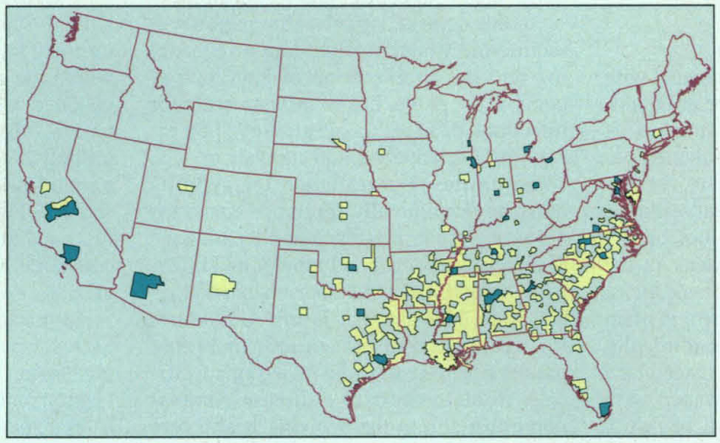
Global disease eradication and disease elimination from localized areas increasingly are being promoted and studied as public health approaches for selected infectious diseases (*1*). However, when a campaign fails, the field can fall into disrepute. Syphilis, identified in the 1930s as the principal public health problem then facing the United States (*2*), was the target of elimination efforts in the 1940s and 1960s, both of which reduced rates substantially but did not succeed in eliminating sustained domestic transmission. Why, therefore, is the U.S. Public Health Service once again targeting syphilis for national elimination?

Rationale for Syphilis Elimination

In the first half of this century, late-stage syphilis was a significant cause of cardiovascular disease and the major cause of insanity and blindness in the United States (*2*). The effectiveness of penicillin and other antimicrobials blunted the impact of late-stage syphilis and helped transform syphilis from a massively endemic disease afflicting as many as 5% of World War II military recruits to a relatively rare sexually transmitted disease (STD) persisting mostly at the margins of U.S. society.

The emergence of the human immunodeficiency virus (HIV) epidemic has greatly amplified the importance of syphilis as a health problem in the United States. Syphilis causes genital ulcers, which dramatically increase the likelihood of sexual transmission of HIV. Syphilis has thus helped fuel the rapidly emerging HIV/AIDS subepidemic in young African-American women in the southeastern United States (*3*). In addition, syphilis can be a severe opportunistic infection with catastrophic neurologic impact in HIV-infected immunosuppressed persons (*4*).

Congenital syphilis is a potentially fatal disease that also can cause severe, persistent neurologic sequelae. It affected more than 3000 infants annually during the peak of the recent U.S. syphilis epidemic of the late 1980s and early 1990s.



CDC STD SURVEILLANCE SYSTEM

Concentrations of syphilis. Counties with rates of primary and secondary syphilis over 4.0 per 100,000 U.S. population (*12*) (yellow) and the 31 U.S. counties that together reported 50% of all U.S. cases in 1997 (blue).

Congenital syphilis inevitably resurges in the wake of syphilis epidemics that include adult women.

The U.S. Department of Health and Human Services has recently established as a priority the reduction in gaps in health status between minority and white populations in the United States. Few gaps in health outcomes currently outstrip the approximately 40-to-1 ratio between blacks and whites in reported primary and secondary (P&S) syphilis in 1997. Some of this gap is attributable to differential reporting of syphilis among blacks to public health agencies. However, most of the differential burden of syphilis reflects the exaggerated multiplicative effects of differences in poverty, health awareness, access to and acceptability of health care services (especially in the rural South), segregated sexual networks, and judgmental attitudes of providers with regard to STDs. This extraordinary differential in a disease that is so susceptible to basic medical care is one of the most glaring examples of existing gaps in minority health status.

Epidemiologic Vulnerability of Syphilis

Syphilis meets all of the basic requirements for a disease susceptible to elimination. There is no animal reservoir; humans are the only host. The incubation period is usually several weeks, allowing for interruption of transmission with rapid prophylactic treatment of contacts, whereas infectiousness is limited to less than 12 months even if untreated. It can be diagnosed with inexpensive and widely available blood tests. In its infectious stage, it is treatable with a single dose of antibiotics. Antimicrobial resistance has not yet emerged.

Since the introduction of penicillin and the organization of a national venereal disease control program in the 1940s, the initial near-elimination of syphilis has been followed by cyclic national epidemics with 7- to 10-year cycles. As of 1997, we were in a period of the lowest incidence ever reported: 3.2 cases per 100,000 people. Moreover, more than 50% of the 8551 cases of P&S syphilis in 1997 occurred in just 31 (1.0%) of the 3115 U.S. counties (see the figure).

The sharply reduced overall number of syphilis cases and their concentration in a handful of endemic areas dramatically diminishes the scope of efforts needed as compared with the much more complicated disease control situation we would face if we were to return to the syphilis rates of 1990 (>20 cases per 100,000 people). The epidemic potential of syphilis is one of the critical reasons why elimination rather than enhanced control is necessary: There is no previous U.S. experience that control of syphilis at low levels is feasible without periodic major epidemics ensuing.

Syphilis as a Social Disease

Few diseases have more complex, stigmatizing social determinants and ramifications than does syphilis. These include the sexual transmissibility of syphilis, its association with prostitution and substance abuse, and the ethnic and socioeconomic disparities in its distribution. Stigmatization complicates every aspect of its control and elimination. Many in the African-American community would consider that even successful elimination of syphilis might not warrant the effort unless it can simultaneously help remedy the public

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health legacy of discrimination and empower communities to deal more effectively with infectious diseases.

Because of the notorious Tuskegee Study (*5*), in which treatment was withheld from black men with syphilis, the stigma extends to the agencies of the U.S. Public Health Service, including the Centers for Disease Control and Prevention (CDC), which funded and supervised the study. The Tuskegee Study has become a principal symbol of unethical research and governmental lack of concern about the fate of its most vulnerable citizens. One result has been the crippling of syphilis research and prevention programs, in part because of shame, distrust, and lack of frank dialogue and leadership. Last year's presidential apology for the Tuskegee Study was an important first step in addressing this legacy of distrust.

Other Barriers to Elimination

In addition to the problems associated with syphilis as a social disease, there are multiple difficulties in the elimination of syphilis. Major outbreaks continue to occur, providing sparks to ignite further transmission to other areas. Surveillance for syphilis, the fundamental tool of any disease elimination effort, is weak in the United States and weaker in endemic areas. Access to good-quality health care is often problematic, and shifts of economically disadvantaged populations to managed care have typically not been undertaken with communicable disease control in mind. Timely and efficient treatment of sex partners has eroded in many areas. There is a large reservoir of infection in other parts of the world, and reimportation will remain a threat. Finally, there are many competing priorities, including many public health priorities, that will make it difficult to maintain sufficient funding.

New Scientific Advances

Fortunately, several new scientific advances are likely to facilitate a renewed effort to eliminate syphilis in the United States. New treatment regimens for syphilis that are currently in development may eliminate the need for injections and the potential for severe allergic reactions that complicate penicillin therapy (*6*). New diagnostic tests now in development use saliva, which may allow outreach into affected communities by nonmedical workers without the risk of puncture injuries from needles.

Most far-reaching in scope, the sequencing of the *Treponema pallidum* genome has been completed (*7*). This landmark project has led to rapid advances in the development of approaches to identifying strains or subtypes of *T. pallidum* (*8*) that will provide critical new tools for epidemiologic studies of syphilis. The development of additional diagnostic tests, therapies, or vaccines may follow, perhaps helping to promote syphilis elimination to a broader, international community.

Strategies

The design challenge for syphilis elimination will be to efficiently pursue the elimination of one microbe (a focused or "vertical" outcome) predominantly through integrated or "horizontal" strategies that reduce STDs in a general way and that more broadly enhance community health in the distressed communities where syphilis persists. Furthermore, this effort must be undertaken jointly by affected communities and public health agencies in a way that shares both control and responsibility.

In this context, syphilis elimination will require the 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 U.S. communities. Surveillance for syphilis must be dramatically upgraded and supported by modern information technology. The capacity to respond rapidly and effectively to outbreaks must be enhanced at local, state, and national levels. Guidelines for treatment and prevention, including partner services, must be reviewed specifically in the context of a disease elimination effort and in the evolving health care environment of the United States. Protocols for community assessment to identify local barriers, opportunities, and potential partners for prevention need to be developed, disseminated to key communities, and supported by training and technical assistance. A distinct program component should focus on preventing the reemergence of syphilis in major cities with documented potential for epidemic transmission of syphilis. Research must be continued and intensified, including behavioral and social policy research as well as biomedical, health services, and epidemiologic research.

This strategy is in accord with recent policy statements that disease eradication and elimination efforts should be designed specifically to reinforce basic health care and public health systems, not to undercut them as vertical or detached elimination efforts for single pathogens may tend to do (*1*). Syphilis elimination should help build the public health infrastructure for early detection of other infectious diseases, such as AIDS, other STDs, and tuberculosis, that thrive or threaten to reemerge in the same marginalized domains as has syphilis (*9*).

Prospects

Why, with respect to syphilis elimination, is 1998 different from the 1940s and 1960s? Most important, the HIV epidemic has given new urgency to elimination. It has led to heightened societal awareness about risky sex and to increased protective behaviors that buttress the prevention of all STDs. In addition, new biomedical and public health tools are available or in development that will greatly facilitate syphilis prevention. At the same time, we can use recent lessons and insights about community mobilization (*10*) to address diseases affecting marginalized populations. Finally, the lesson that infections such as syphilis and tuberculosis will resurge if not addressed in a vigorous and sustained way has been convincingly demonstrated.

The cyclic nature of syphilis in the United States gives us a brief window of opportunity to accomplish elimination within the scope of resources currently envisioned. CDC has estimated that an elimination effort would require at least $25 million annually for 5 years, matched by a parallel allocation of state and local resources. This would be not only a cost-effective but a cost-saving enterprise, as compared with the $80 million annual cost of syphilis treatment alone (*11*).

Elimination of syphilis from the United States would be a far-reaching accomplishment, not only in terms of HIV prevention and maternal-infant health, but for us as a society. We are at an epidemiologic crossroads. The biomedical tools are available and will soon be augmented by additional technologies, including those issuing from the sequencing of the *T. pallidum* genome (*8*). Whether we can use our tools and insights to break the barriers of stigma and discrimination and whether we can sustain our commitment are the questions that must be answered.

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