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## Syphilis on the Rise What Went Wrong?

Meredith E. Clement, MD; Charles B. Hicks, MD

**As the 1990s ended**, syphilis was on the decline. At least in part due to safer sexual behaviors prompted by the AIDS epidemic,<sup>1</sup> the rate of incident syphilis declined to **fewer than 4 cases per 100 000 by the year 2000**,



**a historic nadir**. Eradication of *Treponema pallidum* infection in the United States seemed quite possible through concentrated public health efforts in a relatively small number of high-incidence US communities, and the Centers for Disease Control and Prevention (CDC) was developing a national syphilis elimination plan.<sup>2</sup> Timing seemed auspicious for eradication efforts to be successful. **Now, in 2016, hopes for eradication have long since faded**, as have many of the gains realized by the effort. Rates of syphilis have trended steadily upward since 2000, and the CDC's syphilis elimination efforts officially ended as of December 2013.

The current resurgence of syphilis is particularly disheartening given the tools available to control the infection and the significant benefits of doing so, as noted in the US Preventive Services Task Force (USPSTF) Recommendation Statement in this issue of *JAMA*.<sup>3</sup> The following 3 main conclusions of the USPSTF are based on the available evidence and a commissioned systematic review of studies<sup>4</sup> published since the previous USPSTF statement from 2004.

First, the USPSTF found "screening algorithms with high sensitivity and specificity are available to accurately detect syphilis."<sup>3</sup> Although culture of pathogenic *T pallidum* remains impossible for clinical microbiology laboratories, accurate and inexpensive serologic testing is widely available, even in resource-constrained areas. **For the most widely used treponemal and nontreponemal serologic tests, specificity is in the 98% to 100% range, and sensitivity, which varies depending on syphilis stage, is also quite high.**<sup>5</sup>

Second, "treatment with antibiotics can lead to substantial health benefits in nonpregnant persons who are at increased risk for syphilis infection by curing syphilis infection, preventing manifestations of late-stage disease, and

preventing sexual transmission to others."<sup>3</sup> **Treatment of early syphilis with single-dose intramuscular administration of penicillin G benzathine is highly effective and has the advantage of assured adherence. Success rates for patients receiving this regimen are in the 90% to 100% range**, depending on the stage of syphilis at the time of treatment. Successful treatment prevents progression to late-stage disease, a cause of potentially profound morbidity that can affect up to 15% of persons with untreated syphilis. Early diagnosis and treatment as facilitated by screening programs is preferable to later-stage treatment in which management recommendations are largely based on expert opinion and experience rather than rigorous clinical trials.<sup>6</sup>

Third, the USPSTF found **"no direct evidence on the harms of screening for syphilis in nonpregnant persons who are at increased risk for infection."**<sup>3</sup> The risks of not screening are clear: ongoing transmission of *T pallidum* (thus sustaining the epidemic) and a population of untreated, infected persons at risk for significant and progressive cardiovascular and neuropsychiatric disease. These risks more than outweigh the perceived harms associated with screening, mostly issues related to stigma and patient anxiety in the case of false-positive results. Although not inconsequential, these negatives can be minimized by careful attention to patient confidentiality and clear explanations about the characteristics of the tests used in screening.

All of these points lead to the clear conclusion that "the net benefit of screening for syphilis infection in nonpregnant persons who are at increased risk for infection is substantial."<sup>3</sup>

Based on these readily apparent observations and the conclusion that naturally follows, control of syphilis in the United States seems quite possible, perhaps even easily achievable. Yet evidence from the last 15 years indicates quite the opposite to be true. Why is this so? What has gone wrong?

**Missteps abound** and unforeseen events have undermined control efforts. Consider the following 3 points.

First, interest in and funding for public health measures have diminished, including those designed to address preven-

tion of sexually transmitted infections (STIs). **Funding for public health over the past decade has not kept pace with the growing need.** The CDC's budget has decreased significantly, from \$7.07 billion in fiscal year 2005 to \$5.98 billion in fiscal year 2013.<sup>7</sup> Similarly, state and territorial health agencies have experienced substantial cuts to public health programs, including services for STIs.<sup>7</sup> These funding shortfalls were exacerbated by the economic recession of 2008-2010, **such that by early 2010, more than half of local health departments in the United States were experiencing reductions in their core funding.**<sup>8</sup> In many communities, STI management and prevention are centered in local health departments, and their efforts have been seriously undermined by loss of financial security.

Second, sexual attitudes and behaviors have changed among men who have sex with men (MSM), the highest-risk group for both syphilis and HIV infection. The early years of the HIV epidemic engendered significant behavioral changes, particularly among MSM. These changes included increased condom use, reduced numbers of new sexual partners, and closure of some facilities where HIV transmission was common. Captured in the term "safe(r) sex," these changes also favorably affected rates of other sexually acquired infections. Clearly the perceived risks and consequences of becoming infected with HIV were strong motivators for avoiding risky behaviors. However, as improvements in antiretroviral treatment accelerated, images of young men dying of AIDS largely disappeared, and the fear of AIDS receded, which was accompanied by significant declines in the previously adopted safer-sex behaviors. At the same time, use of the internet as a means of sexual partner identification surged, an event associated with higher-risk sex, including multiple sex partners, unprotected anal intercourse, and greater likelihood of substance abuse during sex.<sup>9,10</sup> **The effect on syphilis was quickly clear in San Francisco, where an outbreak of early syphilis among MSM was directly linked to an online chat room.**<sup>11</sup>

In addition, the use of antiretroviral drugs in HIV-uninfected persons for preexposure prophylaxis (PrEP) and the practice of "serosorting" (selection of sexual partners of concordant HIV serostatus) have both become increasingly common. While almost certainly decreasing the rate of new HIV infections, PrEP and serosorting also likely decreased the rate of condom use, with resultant increased risk of other STIs (including syphilis) in both the HIV-positive and HIV-negative networks.<sup>12</sup>

Third, **focus on HIV infection as a national health priority, while appropriate and productive, reduced concerns about other preventable STIs.** The clinical recognition of AIDS in 1981 quickly led to a substantial and well-funded increase in both research and patient care activities directed to this new disease, perhaps to the detriment of other communicable diseases. Thus, numbers of syphilis cases increased markedly over the following 15 years. The rates of syphilis then declined significantly in the late 1990s for reasons that are not entirely clear,

perhaps only as a consequence of the observed natural periodicity and cycling of syphilis epidemics (thought to be related to changes in host immunity).<sup>13</sup> Whatever the cause, these events may have contributed to complacency and neglect of fundamental public health measures proven to reduce the numbers of new syphilis infections.

The good news is that **fixing what has gone wrong does not require huge capital investment,** breakthrough technological advances, or massive restructuring of our health care system. Improvements are at hand and require mostly focus and commitment on the part of the health care community. First, awareness of the problem needs to be increased, particularly in clinical settings where patients at higher risk for syphilis are being followed up. These high-risk populations include MSM, HIV-infected persons, and younger sexually active persons, particularly persons of color and those from socioeconomically disadvantaged populations. **The syphilis demographic overlaps considerably with the HIV demographic.** For example, in 2014, half of all MSM diagnosed with syphilis were also coinfecting with HIV.<sup>14</sup> Younger men (aged 20-29 years) have a prevalence rate nearly 3 times that of the national average for men, and persons of color are particularly at risk, with black individuals disproportionately affected in the United States.<sup>14</sup> Rates of primary and secondary syphilis were 18.9 cases per 100 000 in blacks compared with 3.5 per 100 000 in whites.<sup>14</sup> Rates in other ethnic groups (aside from Asians, whose rates were lowest of all) were intermediate between blacks and whites.

Furthermore, **health care practitioners need to do a much better job of taking a sexual history and applying recommended screening approaches to the persons for whom they provide care.** Misplaced concerns about patient objections to sensitive questions raise the likelihood of failure to identify high-risk patients and result in missed screening opportunities. Being reluctant or unwilling to ask about sexual behaviors is a disservice to the patient. Clinicians also need to apply the recommendations of the 2006 CDC guidelines for HIV testing<sup>15</sup> as well as the 2016 USPSTF Recommendation Statement on screening for syphilis.<sup>3</sup> Well-planned, periodic screening of persons in at-risk groups, even in the absence of acknowledged risk behaviors, often identifies asymptomatic infections, facilitates treatment, and truncates ongoing transmission.

Although imperfect, serologic syphilis screening is highly sensitive and specific in high-prevalence populations, is inexpensive and technically simple, and has minimal potential for harm. These factors argue for much more widespread and comprehensive screening of groups at high risk for syphilis. Because treatment of early syphilis is also highly effective, identifying untreated infected persons by means of the recommended screening strategy has great potential for both eliminating the consequences of later-stage infection and substantially reducing transmission from those with early infection.

#### ARTICLE INFORMATION

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