Control of Bacterial Sexually Transmitted Diseases in the Developing World Is Possible

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(See the article by Paz-Bailey et al. on pages 1304–12)

Paz-Bailey et al. [1] provide evidence from yet another country of the feasibility of moving from a situation of poor sexually transmitted disease (STD) control, characterized by high prevalences of curable bacterial and protozoan STDs, to one of lower prevalences. An important feature of this change is a decrease in the number of cases of genital ulcers and a predictably changing etiology; as control measures (most effective against bacteria) decrease the proportion of genital ulcers due to Haemophilus ducreyi (in particular) and Treponema pallidum, ulcers of herpetic origin become predominant. This transition toward STD patterns typical of industrialized countries is good news, in that interventions are having an impact on STD transmission and, surely, their sequelae (e.g., infertility), and are likely decreasing the rate of HIV transmission as well.

The decreased prevalences of gonorrhea (68.1%), chlamydial infection (55.0%), and trichomoniasis (65.4%) in the cross-sectional surveys of persons practicing family planning between 1993 and 2002 was considerable, whereas the decrease in the seroprevalence of syphilis (91.7%) was spectacular. For genital ulcers, because only proportional data regarding individuals seeking care were available, one can ask, “Did the number of cases of genital ulcers with a bacterial etiology decrease, or did the number of cases with a viral etiology increase?” A decrease in the absolute number of cases of genital ulcers is supported only by surveillance data, which is often of uncertain quality in the developing world. But control of bacterial genital ulcers is apparent from the magnitude of change in the relative proportions of etiologies of genital ulcers. Chancroid was the most common cause of genital ulcer disease in 1993, yet it became a rare event by 2002; meanwhile, syphilis was disappearing among all patient groups.

Bringing chancroid to near extinction is possible [2]. Because it is characterized by very painful lesions and asymptomatic carriage is rare, it exists only in communities where access to health care services is extremely poor; individuals with chancroid simply will not tolerate the disease unless they have no alternative. Indeed, chancroid can be seen as the riskiest of all STDs (the core of the core), associated with the highest risk behavior. Chancroid thrives under conditions of risky sexual behavior, in which use of condoms is infrequent and sex workers have limited access to preventive and curative services.

A high prevalence of chancroid in a community is an indicator of high-risk sexual behavior and the absence of good medical services. Conversely, the disappearance of chancroid from the community, as it occurred in Botswana, must indicate improvement in safe sexual behavior, better medical care, or both. The health care service control of other STDs, which are more frequently asymptomatic, requires more than just the provision of acute medical services for symptomatic infection (i.e., screening and partner notification services, the only 2 means of reaching asymptomatic individuals).

What led to the epidemiologic changes in Botswana is uncertain. The improvement in safe sexual behavior noted by Paz-Bailey et al. [1] is a possible reason. And, likely, over the 9-year period between surveys, sex work became safer, conditions improved for migrant mine workers, and inroads were made to improve medical care for the general population. That high prevalences of gonorrhea, chlamydial infection, and trichomoniasis persist (although they have decreased from previous levels), indicates that there is further progress to be made, although knowing how to end the “hyperendemic phase” of STDs described by Wasserheit and Aral [3] may not be entirely clear [4].

In the face of the decreasing prevalences of bacterial and protozoal STDs in Botswana, viral STDs, specifically genital herpes, could be more common now than
they were in 1993. Modeling of transmission dynamics of genital ulcers in sub-Saharan Africa has shown that changes in sexual behavior can lead to findings similar to those of Paz-Bailey and colleagues: large decreases in the proportion of ulcers due to chancroid and syphilis, with genital herpes becoming the predominant ulcerative disease [5]. Although there are no data regarding the seroprevalence of HSV-2 infection in Africa during the time period of the HIV infection epidemic [6], that sub-Saharan Africa has the highest prevalence of HSV-2 infection of any geographic area in the world [7], with a prevalence among adults as high as 80%, suggests that any considerable recent increase in the prevalence of genital herpes came not from increased transmission of the virus, but rather from the enhanced clinical expression of subclinical infection caused by increasing HIV infection rates.

Genital herpes facilitates transmission of HIV [8], whereas increasing rates and the duration of HIV infection in the population facilitate clinical expression and the duration of latent HSV-2 infection [9]. This sets up a vicious cycle of mutual benefit and has led to trials designed to enhance patient benefit and interrupt HIV transmission in sub-Saharan Africa by prophylactic and therapeutic use of antiviral medication; for the latter purpose, preliminary economic modeling suggests that such approaches could be cost-competitive with other approaches to HIV infection prevention [10].

Changing genital ulcer patterns similar to those of Botswana have been reported in other places (Thailand, Cambodia, Namibia, and Uganda) that have had success in reversing generalized HIV epidemics. This is more than coincidence. Fewer genital ulcers means less efficient HIV transmission [11, 12].

Thailand reported large reductions in the incidence of chancroid (95% decrease) and syphilis (69% decrease) between 1987 and 1994 [13]. In 1982, reporting sites observed 3 times as many cases of chancroid (15,762) as they did cases of genital herpes (5090). By 1997, there were 15 times more cases of herpes reported (2402) than cases of chancroid (165), but the number of cases of genital ulcers had decreased to 12% of 1982 levels. Increased condom use among brothel-based sex workers decreased sex work, and better STD services are credited with controlling STDs and reducing the prevalence of HIV infection nationwide [14].

Cambodia took a similar approach to condom use and STD services. In 1996, 8.3% of brothel-based sex workers had a genital ulcer (Caroline Ryan, personal communication). In 2001, the prevalence of genital ulcers among sex workers was only 2.1% [15]. Screening of vaginal swab specimens demonstrated that 2.4% of sex workers were infected with HSV-2, but there was no evidence of *H. ducreyi* or *T. pallidum*. The prevalence of genital ulcer disease among police and military was also low in 2001, and HIV prevalence had decreased in all surveillance populations.

In Nairobi, enhanced interventions to increase condom use, improve STD services, and strengthen sex-worker peer networks significantly decreased the prevalence of bacterial STDs and the sequelae of pelvic inflammatory disease, whereas rates of curable genital ulcers decreased to low levels [4]. Chancroid all but disappeared. A recent study of sex workers confirmed that the incidence of genital ulcers was low and limited to genital herpes; the incidence of HIV infection, previously as high as 50% among Nairobi sex workers, had decreased to only 4% [16].

In South Africa, a common work destination for miners from southern Africa, an intervention for women at high risk in the mining communities documented large reductions in the incidence of curable STDs among women using the services [17, 18]. At the start of the intervention, chancroid was the main cause of genital ulcers among the women, but chancroid was not documented after the third month of the intervention. In miners, the prevalence of genital ulcers decreased by 78% within 9 months after the start of the intervention.

The prevalence of HIV infection, however, did not decrease in Botswana; rather, it increased from 18% among pregnant women in 1992 to 37% in 2003. In Malawi, the same decrease in the prevalence of STDs and increase in the prevalence of HIV infection were observed [19]. There, however, the incidence of HIV infection appeared to be decreasing among younger women during the final survey periods, and it is possible that the same effect is occurring in Botswana, where we do not know when the prevalence of STDs began to decrease. Changes in the incidence of bacterial STDs are to be expected prior to changes in the prevalence of HIV infection, and this is a cornerstone of second-generation surveillance of HIV, for which the prevalences of bacterial STDs are used as one indicator of risk behavior in a community, guiding the success of HIV infection prevention efforts [20].

One bacterial infection with a prevalence that remained constant in the Botswana surveys was bacterial vaginosis; its prevalence during both time periods was high: 47% in 1993 and 49% in 2002. On the basis of a meta-analysis of 19 studies [21], bacterial vaginosis seems to facilitate HIV infection [22] by 60%. Although the magnitude of the effect is modest, the high prevalence of bacterial vaginosis may make it a significant enhancer of HIV transmission in a given population. Because the Rakai intervention trial resulted in decreased prevalences of bacterial vaginosis without lowered rates of HIV incidence [23], the role of bacterial vaginosis (which is highly prevalent in sub-Saharan Africa) in HIV transmission needs to be elaborated further.

Motivated by examples of the impact of interventions for bacterial STDs, the World Health Organization is assembling a 5-year control initiative that targets genital ulcers. The ultimate goals of the initiative are to eliminate chancroid and reduce the prevalence of syphilis and, subsequently, as evidence for new inter-
vention strategies emerges, to institute recommendations for HSV-2 control.

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References