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The Wrong Place at the Wrong Time: Geographic Disparities in Young People's HIV Risk

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Adolescence is a period of multiple transitions; unfortunately, physical maturation often occurs before cognitive maturity, leading to sexual exploration and risk-taking behavior. However, what once could lead to a shot of penicillin or an unwanted pregnancy, could now result in a chronic disease. In this issue of *Journal of Adolescent Health*, Pettifor et al compare the reported sexual risk behavior of two large population-based surveys of youth aged 18–24 years in the United States and in South Africa, with cross-sectional HIV prevalences of <1% versus 10%, respectively (20.8% in South African females) [1]. Surprisingly, the South African youth reported later sexual debut, fewer sexual partners, and safer sex than their American counterparts. The only reported behavior that could account for the vast differences in HIV prevalence was the larger age gaps between South African females and their male partners.

There is some evidence to suggest that there are biological reasons for this difference between behavior and prevalence. As the authors mention, the rates of male circumcision (as in complete removal of the foreskin) are lower in South Africa [2,3], whereas prevalence of sexually transmitted infection (STI) is higher [4,5]. However, even in the absence of STIs, African women have higher inflammation in their genital tracts [6], rendering them more susceptible to vaginal sexual transmission. Subtype C virus causes a more sustained viral peak after primary infection [7], and primary infections are liable to contribute to a large proportion of infections among adolescents and young adults. The frequency of co-infections, such as malaria, helminths, and tuberculosis, could also contribute to higher viral set-points, and therefore higher infectivity [8]. Additionally, sub-type C viral envelope proteins have greater affinity for the core-ceptor CCR5 [9]. CCR5 Δ 32, a genetic form of the coreceptor that is resistant to HIV infection, is less prevalent in African populations [10], and there may be other genetic susceptibilities. Finally, violent and nonconsensual sex against young women is rampant in South Africa and is associated with higher HIV transmission rates [11].

The two surveys in the study of Pettifor et al differed slightly; the U.S. AddHealth survey used computer-administered questionnaires. In South Africa, interviewer-administered questionnaires were used, which may have decreased reporting of risky behavior because of social desirability. Although computer-assisted interviews improve adolescent risk reporting in certain settings [12], it is not necessarily true with sub-Saharan African young people [13]. There were some other differences; in the United States, younger Caucasians responded to the survey, which may have biased results. The AddHealth survey was based on a population of previously enrolled students, whereas the Reproductive Health Research Unit (now Reproductive Health and HIV Research Unit) survey was household-based. In some settings, school-going youth are at lower risk for HIV infection [14,15]. Finally, many Southern African youth believe that anal and oral sex hold lower risk, and therefore engage in these behaviors instead of vaginal sex [16], although Pettifor et al state that the frequency of anal sex in this survey was low. Nevertheless, the higher prevalence of HIV in South

African highlights the enormous risk associated with adolescence in South Africa. It is clearly not what you do but with whom you do it.

There is a state of emergency among teenage girls in Southern Africa. Behavioral change campaigns have failed to demonstrate an effect on HIV incidence in heterosexual adolescents [17] and will not likely have a large impact on adolescents in whom risky behaviors are not the primary problem. In fact, the problems are the following: gender imbalances, nonconsensual or coercive sex [11], lack of self-efficacy of female youth [18], stigma leading to low HIV testing and disclosure rates, and poverty causing transactional and intergenerational sex [19]. These problems are far too large to take on in the short-term.

Multiple biological interventions, by contrast, are known to prevent heterosexual HIV infection, yet their rollout has been excruciatingly slow. Although medical male circumcision reduces HIV acquisition in men by two-thirds [20], few healthcare facilities offer circumcision, and it is widely believed that medical circumcision would interfere with traditional rights of passage of young African men [21]. HIV counseling and testing helps to both decrease risk behavior [22] and to facilitate access to antiretroviral therapy for HIV-positive individuals, which in turn decreases infectivity [23], yet HIV testing is still voluntary in most settings, and should be made mandatory or at minimum opt-out. Treatment of STIs for both HIV-infected and negative persons decreases HIV transmission in certain settings [24]. However, only a few truly adolescent-friendly HIV or STI testing or treatment centers exist in Southern Africa [25]. HIV counseling and testing in South African schools has been stalled by much debate and some resistance [26].

Promising interventions that address poverty and gender inequities include unconditional or conditional cash transfers (CCTs) and vaginal microbicides. CCTs have worked for smoking and alcohol use in adolescents, and are even more likely to be successful in cases where lack of money may contribute to the risky behavior. Although there have been some failed attempts at using CCT to reduce HIV infection in adults, cash transfers given to adolescent schoolgirls in Zomba, Malawi, reduced HIV prevalence in the intervention group by 60% [27]. The intervention decreased the risk profile and mean age of the male partners. Valid questions arise regarding the sustainability of the effects of such an intervention, but even short-term effects that curb incidence would be beneficial. Topical vaginal tenofovir gel decreased HIV acquisition by 54% in adherent adult women in South Africa [28]. Although adherence may be lower in adolescents (studies in adolescents are underway), vaginal gels are under control of the female, potentially circumventing gender inequities.

Mother-to-child-transmission prevention programs have been hugely successful in Africa, where evidence-based interventions have been implemented based on accumulated evidence. The World Health Organization changed their infant feeding guidelines to recommend nevirapine to the infant for the duration of breastfeeding to prevent breast milk HIV transmission very soon after the results of the PEPI-Malawi and SWEN studies were released, even without evidence for the efficacy of nevirapine beyond 14 weeks [29–31]. South Africa rapidly adopted this recommendation for infants [32]. How much more evidence do we need before we implement proven interventions to prevent this rampant heterosexual HIV transmission to our youth?

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