HIV Chemoprophylaxis for Adolescents: Educable Moment, Not Magic Bullet

Kenneth H. Mayer¹²³ and Brian C. Zanoni⁴

¹The Fenway Institute, Fenway Health, ²Division of Infectious Diseases, Beth Israel Deaconess Medical Center, ³Department of Medicine, Harvard Medical School, Boston, and ⁴Ragon Institute of Massachusetts General Hospital, Massachusetts Institute of Technology, and Harvard, Charlestown, Massachusetts

(See the HIV/AIDS Invited Article by Pace et al on pages 1149–55.)

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The shape of the human immunodeficiency virus (HIV) epidemic is becoming bimodal because of increasing incidence among young people and the aging of persons infected long ago who are living longer because of access to highly active antiretroviral therapy (HAART) [1–3]. Globally, almost one-half of new HIV infections are occurring among adolescents, and in the United States, the subpopulation with the greatest recent increase in HIV infections is youth from racial and ethnic minority communities [1–5]. A recent 6-city study of black men who have sex with men found that annualized HIV incidence approached 6% among men aged <30 years, exceeding rates seen in many sub-Saharan African countries [6]. Although condom promotion, health education, and behavioral interventions have been shown to decrease risk-taking behaviors among some youths some of the time [7–13], the current array of social and behavioral interventions have not been sufficiently effective, or reached a wide enough population effect, in order to have an impact on the HIV epidemic in youth [3, 4, 14]. In the absence of immediate access to a highly effective preventive vaccine, clinicians and public health workers need to pay increasing attention to the judicious use of antiretrovirals for prevention. The most effective result in this regard was seen in the HPTN 052 trial, which demonstrated that HIV-infected persons were 96% less likely to transmit HIV to their primary partner when they were on HAART [15]. However, even in this study, where both partners had to sign an informed consent (suggesting stable relationships), >25% of the seroconversions were not associated with primary partners [15]. In populations where HIV remains highly stigmatized and serostatus disclosure remains uncommon, relying on treatment as prevention to stop the spread of HIV in young people may expose high-risk youths to unnecessary levels of risk.

In less than 3 years the efficacy of antiretroviral chemoprophylaxis, also known as preexposure prophylaxis (PrEP), has been demonstrated in trials involving heterosexual HIV-discordant couples [16], young women [17, 18], and homosexual men [19, 20]. The effect sizes of the protective benefit have varied and some of the studies did not demonstrate efficacy. Although medication adherence (as measured by serum drug levels in the blood and genital tract) appears to play a pivotal role in whether trials demonstrated PrEP efficacy [20, 21], other factors, such as tissue pharmacology and host mucosal responses, deserve further careful evaluation. Moreover, now that there is proof of concept for the use of oral, daily PrEP with tenofovir and emtricitabine, new studies are under way to determine whether more parsimonious dosing (because many individuals may not be engaging in risk every day), different drugs (to minimize the risk of cross-resistance and to avoid some toxicities), and different delivery systems (eg, modalities that are less dependent on adherence such as intravaginal rings or periodic injections) may obviate some of the concerns raised in the earlier studies.

Therefore, given some of these uncertainties about the optimal way to use chemoprophylaxis, should PrEP implementation be delayed for adolescents? In an article in this issue of Clinical Infectious Diseases, Pace et al discuss why PrEP may offer new opportunities to prevent HIV spread among a new generation of young people, while discussing the challenges to optimal implementation
Given the rates of new HIV infections in some subpopulations, the addition of any proven prevention modality is desirable, but many clinical and behavioral questions regarding PrEP use in youth remain unanswered. One of the statistically significant, but not clinically meaningful, findings in some of the PrEP studies was that bone demineralization was increased in some individuals who were assigned to tenofovir-based regimens [23]. The follow-up in these studies and the number of youths enrolled has been relatively modest to date, such that further long-term assessment of bone mineral density in youths using PrEP is essential to minimize future unintended consequences. Two new studies in the Adolescent Trials Network will enroll 300 youths between the ages 16 and 24, and will include longer-term safety assessments. Further studies of male and female youths recruited in international settings are also needed, given the variability in genetics, diet, and environmental factors that might impact their vitamin D and calcium levels and bone metabolism.

Another unique challenge to wider implementation of PrEP for adolescents is the question of parental involvement in this biomedical intervention. For sexual and gender minority youths, acknowledgement of their behaviors (eg, homosexual or premarital heterosexual relationships) could result in parental abuse, rejection, and economic uncertainty [24]. It is important for public health officials to create a regulatory environment where youths can be evaluated for PrEP as part of a comprehensive prevention program without requiring invariable parental involvement. In the analogous situation of access to contraceptive services, although researchers found that parental consent prior to receipt of hormonal contraception was not an impediment for the majority of the young women surveyed, a substantial minority did report that this requirement would have led them to engage in unprotected sex in order to avoid parental involvement [25]. Regulatory authorities in different jurisdictions will need to review their statutory requirements in order to optimize young people’s engagement in biobehavioral HIV-preventive activities.

PrEP is not an end in of itself, but should be viewed as a new opportunity to develop more innovative and engaging preventive programs for at-risk youth. The advent of the “antiretroviral therapy for prevention” era creates a new imperative for increased HIV testing, as newly diagnosed persons have more reasons for earlier initiation of treatment than ever before and uninfected persons may benefit from new preventive modalities. However, the PrEP pill is not a stand-alone panacea. First of all, not all youths (or others) are engaging in recurrent risk practices that warrant PrEP. Second, the reasons why individuals engage in unprotected sex are diverse, and well-trained clinicians are needed who can take the time to determine if the unprotected sex is in the context of a primary relationship, in which case knowing more about the partner is the first step in advising HIV prevention. For other youths, ongoing risk may be due to untreated depression, which may in itself be due to internalized homophobic because of family and/or peer rejection. Substance use and/or economic necessity may be associated with unprotected sex, so it may be important to address these root causes to minimize risk, rather than just prescribing a pill.

The challenge for clinicians is that the advent of this new preventive modality requires thoughtful discussion to understand who might benefit, and why some youths engage in risk. Discussions about chemoprophylaxis should be part of candid conversations that enable providers and patients to develop HIV prevention plans, which should include behavioral interventions that can be combined with PrEP. At the same time, because PrEP is active only against HIV, youths who are using PrEP need to undergo regular screening for other sexually transmitted infections. PrEP by its nature is a biomedical intervention requiring trained and knowledgeable staff, but it may also present an educational opportunity in which clinicians can learn the reasons why youths are engaging in risky behavior and can then offer supports that may help them avoid future risks. Helpful services may include triaging youths to counseling with mental health professionals, or referring them to social services that can improve their living circumstances (eg, stable shelter, job training). In an era of decreased time and limited resources in the healthcare system, it will be challenging for providers to assess youths’ risk and to offer them preventive modalities, but the prospect of more youths becoming HIV-infected should be less acceptable. Hopefully, as in the case of many new biomedical interventions, early-adopter health professionals may develop best practice models that can become replicated and disseminated to make the PrEP encounter less onerous for less experienced clinicians, while at the same time optimizing the potential efficacy of this new intervention with informed counseling and social service referrals.

Note

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References


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