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HIV Prevention: Great Achievements, More Challenges Ahead

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The response to the HIV epidemic has made remarkable advances in the past decade with expansion of access to HIV care and treatment for populations that had hitherto no hope of such treatment.¹ At the same time, it is heartening to note that after many years of limited progress, the field of HIV prevention has been greatly energized by several recent findings. The dawn of the recent optimism began with the release of the results in 2005 and 2007 of three randomized clinical trials that demonstrated the efficacy of voluntary medical male circumcision (VMMC) for prevention of HIV acquisition by heterosexual men in sub Saharan Africa, highlighting this intervention as a potential “surgical vaccine”.^{2–4} CAPRISA 004 demonstrated the efficacy of vaginal tenofovir gel for the prevention of HIV acquisition by women in South Africa, providing the long-awaited proof of concept for the use of topical microbicides as pre-exposure prophylaxis (PrEP).⁵ This finding was followed closely by other evidence of the efficacy of oral antiretroviral drugs for PrEP in men who have sex with men (MSM),⁶ discordant couples⁷ and heterosexual women.⁸ Concomitantly, the HPTN 052 study generated further excitement with the demonstration of 96% prevention of the sexual transmission of HIV in heterosexual discordant couples in whom the infected sexual partner was on antiretroviral therapy (ART).⁹ The latter findings lent credibility to mathematical modeling research which indicated that expansion of ART could provide substantial impact on HIV incidence.^{10,11}

However, the news has not been consistently positive. Further studies failed to confirm the efficacy of oral and topical PrEP due to limited adherence to the antiretroviral regimen provided.^{12,13} In addition, the recent failure to demonstrate any efficacy of DNA prime/rAD5 boost vaccine candidate in the HVTN 505 Study was a great disappointment.¹⁴

Nonetheless, the sum of successful biological prevention interventions served to inspire the concept of combination prevention in which behavioral and biological interventions are integrated into one strategy that is tailored to a specific population. Remarkably, the advances in HIV prevention science have inspired political leaders and funders to broadly

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discuss the possibility of an AIDS-Free Generation, an aspiration that would have seemed impossible at the turn of the century. This optimism is also complemented by encouraging advances in the search for a cure for HIV infection itself.¹⁵

Yet, this optimism needs to be balanced with sobering facts. Remarkable achievements have been accomplished in terms of scale-up of HIV treatment with approximately eight million individuals accessing ART by the end of 2011.¹ Similarly, the annual number of new HIV infections has decreased by 50% in 25 countries including 13 countries in sub Saharan Africa. However, the total numbers of new infections globally remains staggering, with an estimated 2.5 million HIV infections noted in 2011, about 7000 per day. In addition, in certain regions of the world, HIV incidence continues to rise including in Eastern Europe, Central Asia, the Middle East and Northern Africa, while the vast number of new infections continues to occur in sub Saharan Africa.¹ In the United States, while the annual number of new HIV infections has been stable for the past decade, HIV incidence rates among MSM and particularly Black MSM is alarming and the epidemic remains entrenched.¹⁶ Global prevalence of HIV in MSM, injection drug users and sex workers is equally alarming while young women from southern African countries are acquiring HIV infection at staggering rates.¹ Thus, there is an urgent need to apply the knowledge we have to find ways to implement the available efficacious prevention methods to the populations at risk and to demonstrate the effectiveness of such strategies while at the same time continuing the momentum to identify new prevention methods through continued research efforts.

In this supplement of the *Journal of Acquired Immunodeficiency Syndrome*, authors from diverse backgrounds, differing scientific expertise and disciplines came together to contribute to a compendium on the state of HIV prevention globally. Topics included in this *supplement* range from prevention of HIV in specific populations such as adolescents, women, MSM, drug users to discussions of specific methods for prevention such as HIV testing, pre-exposure prophylaxis, topical microbicides, treatment as prevention, prevention of mother to child transmission and male circumcision. Other articles address key challenges facing researchers such as the design of PrEP studies in the context of availability of an efficacious product, the use of integrated strategies for prevention that include multiple interventions that are tailored to the needs of specific populations, innovations for cross sectional estimation of HIV incidence, ethical issues raised by the use of pre-exposure prophylaxis for prevention, the role of social and behavioral sciences in trials of biomedical prevention interventions and a new paradigm for behavioral interventions for prevention and treatment of HIV. Important issues addressed in other articles include acute infection, pharmacology of antiretroviral drugs in mucosal tissues and the future of phylogeny in HIV prevention research. Finally, the *supplement* also includes an article describing an innovative concept related to the HIV care cascade and another on the role of advocacy for prevention in this new era. Each of the articles highlights what has been achieved, remaining gaps in knowledge and provides an agenda for future research endeavors. The articles also indicate the large gap that remains between proven interventions and their implementation and scale-up within programs. A recurring theme is the importance of measurement and modeling and critical importance of evaluating the effectiveness of combination strategies that include multiple interventions.

Much work remains to be done to better understand the factors that place individuals and populations at risk, to identify safe, acceptable and cost-effective prevention methods and to evaluate and implement these interventions, either alone or in combination, where they are most needed. Even in settings where prevention interventions may be available, there is the need to generate demand for these interventions and to enable those who avail themselves of such interventions to be able to adhere to them in an ongoing manner. It is only through a

continued commitment to HIV prevention that we will be able to conquer the HIV epidemic and declare it as a thing of the past.

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