

# Toward an AIDS-Free Generation

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SINCE THE FIRST CASES OF WHAT IS NOW KNOWN AS AIDS were reported in 1981, an entire generation has grown up under the constant cloud of this modern-day plague. Across the globe, more than 34 million people are living with the human immunodeficiency virus (HIV), the virus that causes AIDS, including approximately 1.2 million individuals in the United States.<sup>1</sup> HIV/AIDS has been responsible for the deaths of an estimated 30 million individuals. Although the rate of new HIV infections has declined or stabilized in many countries, the disease continues to exact an enormous toll: 1.8 million deaths in 2010 alone, grief and hardship for countless families and communities, and deleterious economic effects as those in the prime of life who lack timely access to treatment are lost to parenting and the workforce. Depending on the region of the world, many die with little or no access to medical care, while others require and receive expensive medical and end-of-life care. Despite these daunting statistics, the fight against HIV/AIDS is currently viewed with considerably more optimism than in years past because powerful interventions have been developed, scientifically proven effective, and refined. If these tools are made widely available to those who need them, an AIDS-free generation may be possible—that is, today's children could one day live in a world in which HIV infections and deaths from AIDS are rare.

Foremost among these interventions is combination antiretroviral therapy, which significantly improves the health and longevity of individuals infected with HIV. Since the advent of antiretroviral therapy, the annual number of deaths due to AIDS has decreased by two-thirds in the United States. Globally, an estimated 700 000 lives were saved in 2010 alone due to the increased availability of antiretroviral therapy in low- and middle-income countries.<sup>1</sup> Important challenges remain—notably finding the resources and developing the infrastructure to provide antiretroviral therapy to the estimated 8 million individuals with HIV infection who need these drugs but are not receiving them. Moreover, in wealthy and lower-income countries, only a minor proportion of those with HIV can navigate the entire HIV care cascade, from testing and diagnosis to accessing and being retained in care, starting antiretroviral therapy at the appropriate time, and

then adhering to prescribed regimens to adequately suppress the viral load.<sup>1</sup> Resources and innovative strategies are essential to find, test, and counsel those with HIV infection; help them remain in care; and derive the maximal benefit from antiretroviral therapy and other HIV/AIDS-related services.

Importantly, antiretroviral therapy can also prevent HIV infection by reducing the amount of virus in an infected person's blood and other body fluids such as genital secretions, making it less likely that the virus will be transmitted to others. A pivotal clinical trial known as HPTN 052 demonstrated that when providing antiretroviral therapy to the infected partner in HIV-discordant heterosexual couples early in the course of disease, the risk of HIV transmission to uninfected partners is significantly reduced when compared with deferring therapy until the disease was more advanced.<sup>2</sup> Modeling data and studies in communities in which antiretroviral therapy is widely available suggest that scaling up antiretroviral therapy for HIV-infected individuals likely will substantially reduce the incidence of HIV infection.<sup>3</sup> Thus, it is imperative to strive for universal access to antiretroviral therapy, both to benefit individuals with HIV infection and to reduce the risk of their sexual partners becoming infected.

Antiretroviral therapy also is highly effective in blocking mother-to-child HIV transmission and helped prevent more than 350 000 infant infections worldwide from 2005-2010.<sup>1</sup> Still, 390 000 infants were infected with HIV in 2010.<sup>1</sup> Clearly, efforts to test, counsel, and provide effective antiretroviral therapy regimens to pregnant women with HIV infection must be enhanced to benefit their health as well as that of their infants.<sup>1</sup> Moreover, reducing HIV infections among reproductive-age women and meeting their family planning needs is essential to eliminate mother-to-child transmission of HIV altogether. In addition to medical and societal interventions, voluntary medical male circumcision—a simple surgical procedure—offers a highly effective and durable way to protect heterosexual men from HIV infection. In 3 large-scale studies conducted in Africa, this 1-time intervention reduced the risk of a man acquiring HIV

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during heterosexual intercourse by 50% to 60%,<sup>1</sup> an effect that actually increased over time.<sup>4</sup> Despite logistical challenges, the scale-up of male circumcision holds great promise as part of a broader HIV-prevention regimen, with the potential to prevent millions of infections.

More recently, findings from large clinical trials suggest that preexposure prophylaxis with oral antiretroviral medications can reduce an individual's risk of acquiring HIV infection. At least 3 randomized clinical trials have suggested that a daily oral preexposure prophylaxis approach may be effective, with better results correlating with higher rates of adherence to the prescribed regimen.<sup>5</sup> Longer-acting antiretroviral drugs, delivered monthly or even less frequently, are in development and may improve adherence. Topical gels containing antiretroviral drugs also have shown promise as HIV prevention tools to be applied to the vagina before sexual intercourse to block the acquisition of HIV.<sup>5</sup> As with oral preexposure prophylaxis, the effectiveness of microbicides likely will in large part depend on adherence to the regimen, which may be facilitated by new technologies such as antiretroviral drug-infused vaginal rings designed for monthly use.

Each of these treatment and prevention strategies has a strong evidence base; with further refinement and scale-up and also when used in combination, they could have an extraordinary effect on decreasing the trajectory of the HIV pandemic. As the global community works to increase global coverage of proven interventions (such as antiretroviral drugs for treatment and prevention and male circumcision), researchers are maintaining focus on 2 key scientific challenges that remain: the development of a vaccine and a cure. A safe, effective, and durably protective vaccine would be a huge boost to HIV prevention efforts, in the same way that vaccines for other important diseases such as smallpox, polio, and measles have greatly reduced or eliminated the burden of those infections. Modest success in a large-scale clinical trial of an HIV vaccine, promising results in animal models, and advances in structure-based vaccine design suggest that an HIV vaccine is feasible.<sup>6</sup>

The prospect of an HIV cure remains challenging.<sup>7</sup> Despite the considerable success of antiretroviral therapy in reducing viremia and improving patient health, it has not been possible to cure an individual of HIV infection—ie, to induce permanent remission in the absence of therapy. Over the past 3 years, an accelerated research effort has been un-

dertaken to elucidate the exact mechanisms of HIV persistence and to develop interventions to eliminate or permanently suppress recalcitrant HIV reservoirs. The effects of a cure would substantially benefit the individual, obviating the need for lifelong daily therapy. In addition, society would benefit because of the reduction in treatment costs and rates of HIV transmission.

The availability of combination antiretroviral therapy for prevention as well as treatment, advances in preexposure prophylaxis with oral or mucosally delivered antiretroviral medications to reduce an individual's risk of acquiring HIV infection, together with scaling up medical male circumcision, services for pregnant HIV-infected women, condom provision, and other proven prevention tools suggest that controlling and ultimately ending the global HIV/AIDS pandemic is possible. Achieving this goal, however, will require implementing a multifaceted global effort to expand testing, treatment, and prevention programs, as well as meet the scientific challenges of developing an HIV vaccine and possibly a cure. Realization of success will require a global commitment of resources involving additional donor countries, strengthening health care systems overall, and fostering greater ownership by host countries of HIV/AIDS effort, including investing more in the health of their people. With collective and resolute action now and a steadfast commitment for years to come, an AIDS-free generation is indeed within reach.

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