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Controlling the HIV epidemic, without a vaccine!

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Despite recent failures of vaccines and microbicides [1], other developments in HIV prevention research give reason for optimism that the HIV epidemic may be controllable – made unsustainable – in some populations. To make full use of new knowledge and technology, efforts at HIV prevention must become more coordinated and focused on clearly defined goals, such as epidemic control, even in the absence of a vaccine.

The increased worldwide availability of HAART provides opportunities to decrease HIV transmission through several mechanisms. Reducing HIV RNA levels in plasma and genital secretions may diminish infectivity, as demonstrated in maternofetal transmission studies and a small, heterosexual transmission study [2]. Studies of nosocomial transmission provide indirect evidence of the efficacy of postexposure prophylaxis (PEP); use of antiretroviral therapy (ART) to reduce risk of heterosexual transmission of HIV is under study. Several modeling studies strongly suggest that lowering the viral load reduces risk of HIV transmission [3], although current treatment guidelines limit access to therapy for this purpose. Current guidelines do, however, encourage testing for HIV infection, thereby providing opportunities for interventions to reduce transmission. Abstinence promotion, herpes simplex virus 2 suppressive treatment, protective immunization, and topical microbicides (studies of ART as microbicide are underway) have not shown much promise in randomized trials, but male circumcision and treatment of concurrent sexually transmitted diseases [4] have shown more promise, as have studies of behavioral interventions such as promoting condom use [5,6]. More broadly, measures such as identification and treatment of people during periods of high infectiousness, education regarding transmission, vigorous contact tracing, and population screening have had major impact on many diseases for which no vaccine is available, including syphilis and tuberculosis [7].

The efficacy of rollout of HAART (and high observed levels of compliance), in developing countries, demonstrates what is achievable through coordinated efforts of governments and nongovernmental organizations (NGOs), aided by lower cost and more widely available laboratory monitoring techniques. Although most research on HIV transmission has focused on chronically infected patients, the importance of the acutely infected is being increasingly recognized [8–10]. Furthermore, the feasibility of identifying individuals with acute or very early infection has been much increased by the success of methods for pooling the required tests, even in relatively low prevalence areas [11–16]. The increased cost of earlier initiation of HAART, though considerable, might, over time, be far outweighed by benefits of reduced

transmission. Because HAART therapy extends life and treatment duration – perhaps by decades [17] –preventing new cases is imperative for cost containment. Consider the simple example of a population with an HIV prevalence of 1000 and an effective HIV reproductive rate above one, that is, 1000 infected people are expected to give rise to at least as many new infections. Suppose patients were to initiate treatment an average of 5 years earlier, adding 5000 person-years of treatment for the original prevalent cohort. Compensating for this additional treatment requires reducing the number of new infections by $N = 5000/Y$, in which Y is the average duration of treatment. For example, for $Y = 25$, $P = 200$, corresponding to no more than a 20% reduction in the number of new cases arising from the original 1000 patients, and preventing each new infection may in turn prevent chains of transmission. The need for lifelong treatment imposes a considerable burden; however, as with gonorrhea and syphilis, focus on acute or very early HIV infection or on those known to have transmitted virus or both, may be the most cost-effective way to target therapy. Given the higher risk of transmission during primary infection that could lead to higher effective reproductive rates [18], cost effectiveness might be enhanced by interrupting treatment of the acutely infected after 1 year and resuming when guidelines are met. Similarly, even if early treatment causes some resistance, this practice might still lead to reduced prevalence of resistant infections if it sufficiently reduces HIV incidence. Appropriate studies are needed to assess costs and benefits of treatment policies in different settings.

Epidemic modeling should also be used to explore synergies and tailor interventions for local conditions. For example, in settings where wives, but not husbands, tend to be monogamous, it may be most cost effective to concentrate efforts on commercial sex workers. Modeling surveillance data makes it possible to monitor whether or not populations are on track to achieve control –information that might be fed back to communities to encourage participation in prevention efforts. Implementation of even only modestly effective, but synergistic, interventions, might make controlling the HIV epidemic a realistic goal.

Achieving the desired level of coordination will not be easy. But it will be necessary for epidemic models to be useful in investigating the impact of interventions and proposing new ones, suggesting research studies or surveillance methods to improve model inputs, and identifying the most cost-effective deployment of resources. Modelers must coordinate their efforts with those needed to mount studies, launch interventions, and evaluate cost effectiveness. Although a safe and effective vaccine must remain a major goal of AIDS research, it is unwise to plan epidemic control efforts on the premise that this goal is reachable, given the daunting challenges to be overcome. While vaccine research proceeds, we must exploit scientific advances already achieved; the means to control the HIV epidemic may already be within our grasp.

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