

Universal Testing and Immediate ART

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The world, and not just South Africa, has failed to contain the epidemic of HIV/AIDS. With one or two exceptions, behaviour change programmes, condom promotion, treatment of sexually transmitted diseases, vaccines and microbicides have not reduced transmission, have not been developed or have even increased the risk of infection (1). Male circumcision appears to be the only fairly certain way of reducing transmission and reduces transmission, averaged over men and women, by about 40% (2). It is, however, clear, that if HIV-positive people are put on anti-retroviral therapy (ART) and are fully compliant, their viral load will fall by a factor of ten thousand to one million times and they will be minimally infectious, if at all. Many are now asking if ART can be used for prevention as well as treatment (3-5).

While much is still unknown about the epidemiology of HIV, the following is certain: South Africa has had one of the fastest growing epidemics of HIV in the world with the prevalence doubling every 18 months. This means that at the start of the epidemic each person infected with HIV was infecting one other person every fifteen months, on average. With a life-expectancy after infection of ten years this means that each person with HIV was infecting about seven people during the course of their infection. To control, and eventually eradicate HIV we need to ensure that each person with HIV infects less than one other person (on average) during the course of their infection. We can achieve this by testing people once a year (on average) and starting them immediately on ART (6).

A policy such as this would have significant and important benefits for South Africa. While HIV-positive people are at much higher risk of developing TB than HIV-negative people they only develop TB eight years after being infected with HIV, on average. Starting people on ART within one year would almost completely eliminate the five-fold increase in TB rates that have happened as a result of the HIV epidemic.

Several objections to the idea of starting people on ART have been put forward. First, there is the issue of cost and affordability. Clearly an intervention such as this would be very costly. If we assume that all six million South African's were started on ART and place the total cost of treatment and care at roughly US\$500 per year, the initial cost would rapidly rise to about US\$3 billion per year. However, this would eventually lead to eradication. The alternative would be to spend somewhat less, perhaps about US\$500 million per year, but to do

this forever with the corresponding loss of life, social disruption, and increases in poverty.

Second, is the issue of human resources. There is a shortage of clinical staff in South Africa and the intervention would have to be made as simple as possible. Since people would be started on ART immediately after they were found to be HIV positive this would eliminate the need for CD4 testing machines, currently one of the biggest obstacles to providing treatment. It is clear that success would depend heavily on our ability to mobilize community workers to educate and inform people, ensure that they have access to testing, ensure that they are able to access their drugs and ensure that they comply with their drugs. One positive feature of the plan is that experience shows that compliance in Africa is generally much higher than in developed countries.

Third is the issue of side effects from drug use. While it is true that some people experience severe allergic reactions to HIV drugs, it would be better to find this out when the person is still in good health so that other regimens can be tried rather than to wait, as at present, until they have serious AIDS defining illnesses, including TB, and then discover that they cannot take the first line drugs.

Fourth is the issue of drug resistance. While some people experience 'viral rebound', the viral load rarely returns to the pre-treatment levels; if the viral load does rebound it generally only returns to about 1% of its original level and the prognosis for people with viral rebound remains much better than for those not on treatment.

The immediate need is to set up perhaps four or five sites in which this intervention can be rapidly but thoroughly tested. We would need to ensure that people are educated and informed, that the projects are owned by the local communities, that there is no stigma and discrimination, that the drug supply is maintained efficiently, that people are compliant, that there is only residual transmission (if any) and that adverse side effects do not compromise the intervention. While carrying out these trials one would simultaneously want to develop a regional plan which could be rolled out as soon as it was clear that the intervention is working, if indeed it is.

While cost remains a major factor there is no doubt that if the pharmaceutical companies were offered secure and predictable markets, they would be willing to substantially reduce the price of first and second line drugs. If an investment of this magnitude is to be made then it must be done in

such a way that it promotes job creation and training in the most affected, which are often also the poorest, communities in the country.

The prevalence of HIV, that is the proportion of people currently infected, is typically about 10% and the incidence of HIV, the proportion of people who are newly infected each year, is about 1% per year. In a trial site of 10,000 people about 1,000 of them would be HIV positive so that the cost of running a site would be of the order of US\$500 thousand per year for about two years. There would then be about 100 new infections per year at current rates. If the intervention works as expected this should fall to not more than 5 new infections per year and the sample size would be large enough to measure the impact.

The National Strategic Plan has set a target to reduce new HIV infections by 50% by 2011 (7). If this is to be done it will be necessary to implement the strategy of universal testing and immediate ART as described here and in a recent correspondence to the Lancet (8). This would entail a massive investment of both money and people and would have to be seen as part of a broader strategy of health system strengthening, social mobilization, community development and rural reconstruction. Most importantly it will need strong and dedicated leadership. But this could also be the beginning of a New Deal for Africa.

Acknowledgement: The author thanks Prof. John W. Hargrove and Dr. Alex Welte for their contributions to the conception of the article.

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References:

1. Padian NS, Buve A, Balkus J, Serwadda D, Cates W, Jr. Biomedical interventions to prevent HIV infection: evidence, challenges, and way forward. *Lancet*. 2008;372(9638):585-599.
2. Williams BG, Lloyd-Smith JO, Gouws E, Hankins C, Getz WM, Hargrove J, de Zoysa I, Dye C, Auvert B. The Potential Impact of Male Circumcision on HIV in Sub-Saharan Africa. *PLoS Medicine*. 2006;3(7):e262.
3. Williams BG, Hargrove J. The case for early antiretroviral therapy for HIV/AIDS. *Quest*. 2008;4:36.
4. Montaner JS, Hogg R, Wood E, Kerr T, Tyndall M, Levy AR, et al. The case for expanding access to highly active antiretroviral therapy to curb the growth of the HIV epidemic. *Lancet*. 2006;368(9534):531-6.
5. Wohl D. Presenting for Care: Too late and with too few CD4+ cells. *HIV JournalView: Top 10 HIV Clinical Developments of 2007*. <http://www.thebodypro.com/content/art45308.html#pub2>. Accessed on February 6, 2009.
6. Granich RM, Gilks CF, Dye C, De Cock KM, Williams BG. Universal voluntary HIV testing with immediate antiretroviral therapy as a strategy for elimination of HIV transmission: a mathematical model. *Lancet*. 2009;373(9657):48-57.
7. Government of South Africa. HIV and AIDS and STI Strategic Plan for South Africa, 2007-2011. Pretoria: Government of South Africa; 2007:119.
8. Williams BG, Ginsburg D, Montaner J, Stander T, Welte A. Achieving South Africa's National Strategic Plan for HIV/AIDS. *Lancet*. 2009;373(9667):895-896.