

HIV prevention - what's new?

Since its identification in the 1980s, the prevalence of infection with the human immune deficiency virus (HIV), the cause of acquired immune deficiency syndrome (AIDS), has increased relentlessly in spite of concerted efforts to curb its spread. The majority (> 90%) of people infected with HIV live in low- and middle-income countries.¹ Poverty, migration and their consequences are plausible explanations for the rapid spread of a disease that is mainly transmitted sexually and through contact with blood. However, they seem inadequate as explanations for the strikingly disproportionate burden of the epidemic in sub-Saharan Africa (which is home to only 10% of the world population yet accounts for over 60% of infected people).^{1,2} More data are needed to elucidate variables for disease spread, particularly those relating to behaviour. What specific behaviours, cultural or otherwise, make sub-Saharan Africans, or any other people, more susceptible to infection? Even though the magnitude of benefit from circumcision is debatable,^{3,4} the lower HIV prevalence⁵⁻⁷ and seroconversion rates (adjusted risk reduction of about 60%)⁸⁻¹⁰ in circumcised cohorts illustrates this point.

The situation is improving, as better treatment becomes available; HIV is no longer the automatic death sentence it was in the early days. Unfortunately the significant strides in drug discovery are only converting HIV into a chronic disease - there is still no prospect of a cure in the foreseeable future. There is no doubt that disease prevention is still the most cost-effective way of dealing with the pandemic. Prevention includes various strategies, such as avoidance of exposure to infection, where avoidance of risky sexual behaviour and the proper use of condoms should be emphasised. And a vaccine would be ideal, especially if a jab could offer lifelong immunity! Another component of prevention is testing, not only so that people know their HIV status but also so that accurate data on the burden of disease are available for public health measures.

Routine HIV screening and testing

At an estimated HIV prevalence of 37% in adults (15 - 49 years) only a few years ago, Botswana had one of the highest prevalences in the world. In January 2004 a new initiative of routine HIV testing was launched, initially in prenatal clinics¹¹ but later extensively. Everyone seeking health care received an HIV test unless they specifically refused. This moved the HIV test from its isolated position to part of the 'routine battery' of tests such as full blood counts. Progress as a result of this initiative has been amazing; the numbers of people who need antiretrovirals (ARVs) and are receiving them increased from 16% in 2004 to 70% in 2006. There are also indications that routine testing is widely supported by Botswana citizens, with 89% of adults offered the test agreeing to participate.¹²

As one who has worked at sexually transmitted infection (STI) clinics, where disease is spoken of openly and partners are called in for treatment, I have always wondered whether, had HIV not initially been associated with homosexual communities, the emphasis on confidentiality would ever have become so significant. In fact, rather than being embarrassed, many men at STI clinics portray confidence, as if the disease was a sign of virility. Perhaps if we had been doing all along

what Botswana is doing now, the stigma and consequent reluctance to test may not have been significant. On the other hand, it is possible that the inevitable death associated with the early HIV epidemic may have been seen as a stigma in itself. We may also not have perfected the necessary skills of counselling (pre- and post-test).

The number of people undergoing voluntary counselling and testing (VCT) in South Africa is increasing.¹³ VCT has been routinely offered to women in prenatal clinics in many countries and has made a major contribution to our understanding of the epidemic. Data also indicate that HIV transmission rates among those who are aware of their HIV status are lower than among those who are unaware they are infected - another potential benefit of testing. Routine screening and testing could potentially increase access to diagnosis and treatment, as even people presenting for minor ailments would be offered the test.

According to Ms Natalie Leon, PhD research fellow with the Medical Research Council, pilot intervention introducing screening for STI clients is being studied at 2 youth clinics (both in Khayelitsha) and 7 adult clinics in the Cape Town metropolitan area. These clinics offer family planning and STI services and are sites where patients presenting with a new STI episode are enrolled for the pilot studies. Routine HIV screening and testing (also called provider-initiated testing and counselling - PITC) differs from VCT in that in addition to testing for diagnostic purposes in patients with HIV symptoms, the test is offered for routine screening in patients without symptoms. The health care provider offers pre-test counselling (that focuses on getting informed consent) and does the finger-prick test, whereas in VCT the health care provider sends the client to a lay counsellor for pre-test counselling but the counsellor is not allowed to do the test. Routine screening has to cover four main areas: offer the test explaining its clinical benefits, inform of right to refuse the test, inform on available follow-up services, and give an opportunity to consider the need to inform people who may be affected by the test result. VCT includes all four of these elements but also gives a lot of information about HIV and takes longer.

In the youth clinic pilots the health care provider, usually a nurse, does the above abbreviated pretest counselling as part of offering a standard STI service, does the finger-prick test and the clinical examination, and can give results and do post-test counselling because the rapid test takes 15 minutes. A patient may be referred for further counselling if necessary. In the adult clinic pilots, because of logistics the results and post-test counselling are given by lay counsellors.

Obvious advantages of VCT are that detailed information is given, and both pre- and post-test counselling are usually performed by the same counsellor. The advantages of routine screening and testing include not only normalising HIV tests, but allowing nurses to engage more with their patients on HIV and making the STI service more integrated and efficient. The outcome of these pilots will show if there is an increase in testing rates and, it is hoped, contribute to the attempt to extend the service beyond STI clinics. No doubt this will raise problems related to counselling and capacity issues at primary health care centres.



HOT TOPICS

The success reported by Botswana calls on us to explore and find an appropriate balance, ideally without losing the benefits of VCT. The latter could allow more accurate estimates of the burden of disease, ultimately improving our national response to the epidemic. Botswana is teaching the world; routine testing for HIV, also known as opt-out testing, is now also being recommended by the Centers for Disease Control and Prevention (CDC)¹⁴ in the USA.

HIV vaccines

One viral disease that has been eradicated successfully is smallpox, and this was achieved through vaccination. The theory behind vaccination seems simple enough – the immune system is exposed to either a dead or live attenuated virus or specific viral antigens, in the hope of stimulating an immune response. When subsequently exposed to a virulent virus the immune system responds speedily, effectively eliminating the virus and preventing disease. So why then is it that after 20 years of research and expenditure of millions of rands there is still no vaccine against HIV?

Genetic diversity

The most useful virus for understanding viral genetic diversity is the flu virus. One flu vaccination does not confer permanent immunity, because with every new season immunogenic antigens mutate. In spite of the fact that the symptoms induced by different flu viruses are similar, the body's ability to kill each therefore requires specific immune responses. Hence the need for repeated flu vaccination in susceptible individuals in order to protect them against the season's prevalent strains.

Summary of HIV vaccines

At a recent meeting at Groote Schuur Hospital, Professor Anna-Lise Williamson of the Institute of Infectious and Molecular Genetics at UCT and the South African AIDS Vaccine Initiative (SAAVI) gave an articulate presentation on the subject.

Some of the characteristics that make it difficult to design an effective vaccine against HIV disease include the fact that HIV not only mutates but integrates with and hides in the host's DNA. In addition, correlates of HIV infection control are undefined and HIV destroys cells of the immune system.

There are two major types of HIV virus – HIV-1 and HIV-2. In South Africa 2 of the possible 9 subtypes of HIV-1 occur, i.e. subtypes B and C, which are responsible for the homosexual and heterosexual epidemics respectively. Subtype C is responsible for 98% of the epidemic in South Africa, is also the dominant subtype in Asia, and is responsible for > 50% of the infection worldwide.

An ideal vaccine would firstly induce neutralising antibodies, thus stopping the virus from entering cells. Secondly it would stimulate cytotoxic T cells to destroy cells infected with the virus. Finally it would prevent infection, or at least lower the viral load and prevent (or slow) progression to AIDS. Most importantly, however, such a vaccine should be safe, with no or minimal adverse effects.

The process of vaccine development is long, about 10 years from basic science to trials (phase 1 - 3) in humans. Testing one strategy at a time would therefore be inefficient, as it is not known which will work. HIV has many genes; an ideal vaccine will include many genes in order not only to be effective in more geographical areas but also to cover the

genetic diversity and mutations within an area. The Gag gene is the most immunogenic.

One of the indications that an HIV vaccine could work is that infected people regulate or cope with their infection for a long time before developing AIDS. In addition, some people are slow progressors, and this has been shown to be associated with the Gag protein. Finally, some people are exposed to the virus but don't seem to get infected – for example some of the babies born to infected mothers, and some sex workers.

The recent press about the MRK Ad5 HIV-1 trivalent vaccine trials, with sites in Johannesburg, Durban and Cape Town, has created a lot of interest. The vaccine utilises a modified adenovirus as a carrier for three HIV-1 subtype B genes, so the subtype may at face value cause concern about likely effectiveness in our predominantly subtype C epidemic. It is hoped that the vaccine will yield useful information about the immunology of HIV, and even if no reduction in the infection rate is noted, disease modification (i.e. prolonged viral load suppression) may be significant. Dr Linda-Gail Bekker, the lead investigator at the Cape Town site, is also concerned about the new Health Act, which will push up the required age for parental consent for inclusion in vaccine trials from the current 18 to 21 years. The latter is inconsistent with the fact that people aged between 18 and 21 years can consent to sex and even have abortions without parental consent. This is also the age group most likely to benefit from a vaccine once an effective one is registered.

In a recent paper Burgers *et al.* write that 'Although there are numerous candidate HIV-1 vaccines entering the clinical-trial pipeline, those based on the subtype B have predominated and are at the most advanced stages of clinical testing despite the burden of new infections being due to subtype C. More recently new subtype C candidate vaccines, containing multiple HIV-1 genes have entered clinical trials.'¹⁵

The good news is that an HIV-1 subtype C multigene vaccine called the SAAVI DNA-C has been developed and successfully undergone preclinical testing; it is the first in Africa.¹⁵ In order to reduce the impact of diversity, the genes included in the vaccine were selected from blood taken from individuals within 3 months of infection and selection was based on closeness to a South African subtype C consensus sequence. Not only is South Africa the first country in Africa to develop and test the first HIV vaccine, the first (phase 1) trials in humans will take place in the near future here and in the USA. The current multi-strategy approach to HIV vaccine development is likely to bear fruit.

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Editor

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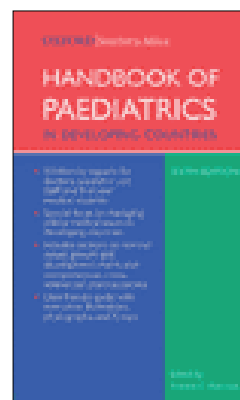
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