are urgently needed for children orphaned by AIDS or living with sick adults.

For such interventions to be effective and accepted, they must be developed through the collaboration of researchers, governments, communities and affected families. So scientists need to focus on the messy, multifaceted social context of the epidemic, not just on the disease itself.

Support programmes must also be properly resourced. Fortunately, organizations such as Save the Children, UNICEF and USAID are already partnering with the governments of South Africa, Swaziland, Malawi and Ethiopia to ensure that essential psychosocial interventions are provided. These include training community care workers in bereavement support.

The evidence as to which interventions are effective is still thin, but we are not starting from scratch. Last year, for instance, a collaborative study involving health practitioners from Uganda and Sweden showed that depression, anger and anxiety lessened in children who had lost one or both parents to AIDS if they had access to support groups and intensive medical care[10].

Lindiwe has told only her brother and us about her diagnosis. She asks whether she could call us if she needs to talk to someone. What Lindiwe craves is affection, acceptance. Her boyfriend loves her but in her township, love is Russian roulette: HIV prevalence in her age group is 25%.

A few days after talking to Lindiwe, I spoke in a government meeting in Johannesburg. I put up a graph showing how non-stigmatized children with enough to eat have a 19% risk of developing a clinical-level psychological disorder; children who are stigmatized and hungry have an 83% risk[4]. I looked up at the audience of senior officials. A few of them had tears in their eyes. We must win this battle. ■

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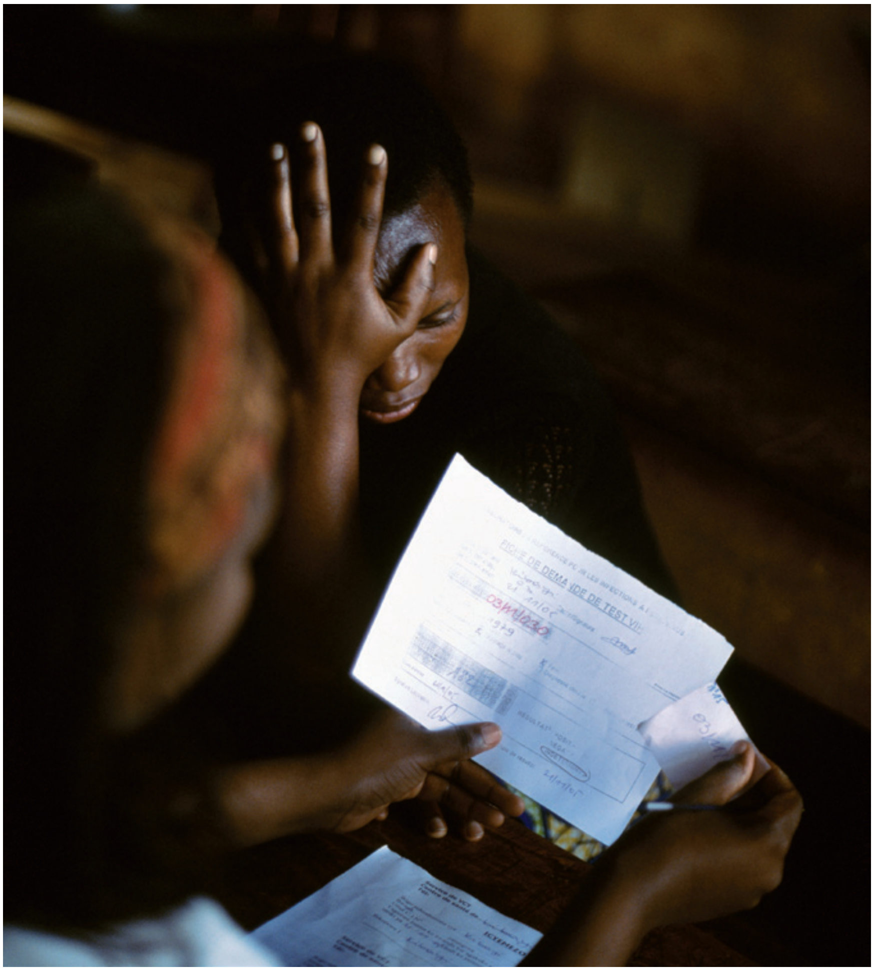


S. FREEDMAN/PANOS

A woman receiving her AIDS test result at Kibayi Health Centre in Rwanda.

Stigma impedes AIDS prevention

Medical advances cannot help those who deny they are at risk of HIV and avoid HIV tests. **Salim S. Abdool Karim** describes how such attitudes may be overcome.

Thirty years since the first cases of AIDS were described, there is much to celebrate regarding progress in the treatment and prevention of the disease. Within the past year alone, several studies have revealed that antiretroviral drugs can prevent the sexual transmission of HIV.

Yet worldwide, many people who are potentially exposed to the virus avoid finding out whether they carry it, or deny that they are at risk of contracting it. Unless people establish whether they are infected, they will not be able to be adopt the most appropriate preventive measures. As scientists and clinicians, our ability to overcome this denialism will determine whether we ultimately succeed in using combinations of all the preventive and therapeutic tools now available to slow, and eventually stop, the HIV/AIDS pandemic.

During its first decade, the disease brought death, pain and suffering, made worse by the stigma that accompanied infection. As a newly qualified doctor in South Africa, it was agonizing for me to watch hundreds of patients die from AIDS — unable to do much more than treat ▶

their tuberculosis or pneumonia infections and make their last days comfortable. Amid this despair, charlatans and 'snake-oil' cures were plentiful. The real hope among the medical community was that science would produce a vaccine or a cure.

This hope was not entirely misplaced. The most significant advance in the second decade of the epidemic was the development of antiretroviral drugs to treat AIDS patients and to prevent pregnant women from passing on HIV to their children. In the late 1990s, 'triple' antiretroviral therapy transformed AIDS from a uniformly fatal condition to a treatable chronic disease — but only in those countries that could afford the roughly US$20,000 a year that it cost to treat each patient.

> *"We must not allow the fourth decade of the AIDS epidemic to be the decade of missed opportunity."*

For Africa, the turning point came in 2000, at the 13th International AIDS Conference in Durban, South Africa, when community groups, activists, patients, scientists and health-care workers jointly protested against drug companies and governments, and called for an end to global inequities in access to AIDS treatment. Within a few years, antiretroviral therapy became a reality throughout most of the continent, mainly thanks to funding from the Global Fund to Fight AIDS, Tuberculosis and Malaria, and the US President's Emergency Plan for AIDS Relief (PEPFAR).

DENYING THE RISK

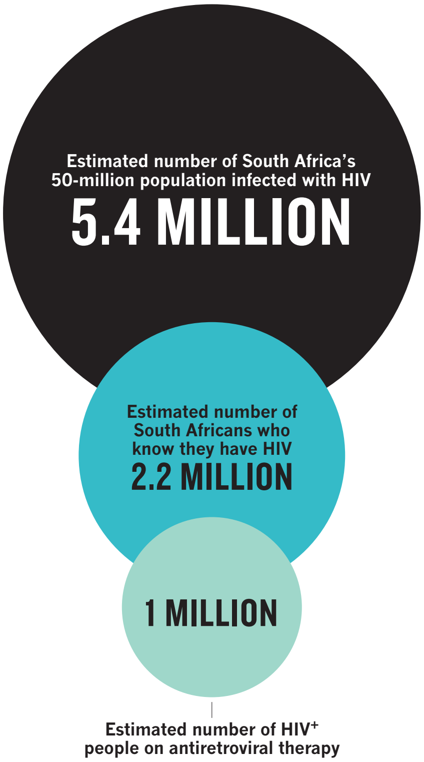
Events took a different course in South Africa, where today 5.4 million people are thought to be infected (see graphic) — more than in any other country. Until 2004, government hospitals were barred from giving antiretrovirals — whether to prevent rape victims from acquiring HIV or to treat patients dying from AIDS. Thabo Mbeki, South Africa's president at the time, denied that AIDS existed. He and his supporters saw the assertion that a new sexually transmitted disease was sweeping through Africa as a racially motivated attack against blacks and a way for pharmaceutical companies to exploit the poor.

Following persistent activism, advocacy, litigation and mass mobilization involving people living with HIV, the Mbeki government eventually initiated a national antiretroviral rollout in 2004. The delay caused an estimated 330,000 unnecessary deaths and some 35,000 avoidable HIV infections in babies[1].

Back in 1999, I was asked to join Mbeki's advisory panel, established to assess whether HIV causes AIDS. Sitting on that panel, engaging in futile debate with AIDS denialists while the epidemic raged on, marked the lowest point in my life. I never imagined that a decade later, long after Mbeki had stepped down, one of the biggest obstacles to curbing the epidemic, both in South Africa and throughout the world, would be another form of denial — this time at the individual and community level. The two kinds of denialism are very different. But both illustrate that scientific knowledge and innovation alone are not enough to save lives.

In the epidemic's third decade, compelling evidence accumulated from clinical trials that male circumcision reduces the likelihood of men contracting HIV from infected women by more than 50%. Last year, my colleagues and I showed that an antiretroviral drug called tenofovir, formulated as a vaginal gel, reduces the chance of heterosexual women contracting HIV by 39% (ref. 2). Also in 2010, epidemiologists showed that a combination of oral tenofovir and another oral antiretroviral, emtricitabine, reduces the likelihood of men who have sex with men acquiring HIV by 44% (ref. 3). Most promising of all, the results of a multinational clinical trial released last month suggest that antiretroviral treatment can reduce the transmission of HIV from infected men and women to their uninfected partners by 96%.

With these tools — circumcision plus antiretroviral drugs that can treat AIDS patients, prevent mother-to-child transmission of HIV and block the sexual transmission of the virus — stopping the epidemic is within our grasp. But only if more people acknowledge their risk of contracting HIV and find out whether they carry the virus.



Acknowledging infection risk is a first step to getting tested for HIV or taking precautions. Risk awareness must be sustained, as taking preventive antiretroviral pills or applying the microbicidal gel inconsistently can lessen their effectiveness. Also, it is crucial that people who do take preventive measures know whether they already carry HIV, because exposing infected individuals to a single antiretroviral drug designed to prevent uninfected people from contracting the virus could facilitate the emergence of drug resistance.

Moreover, when people know they have HIV, they may be less likely to pass on the virus to uninfected partners. For instance, American men and women who are unaware that they carry HIV are 3.5 times more likely to transmit the virus to others than those who know they are infected[4].

GETTING TESTED

Ensuring that people are sufficiently aware of their level of risk and that they seek regular testing for HIV has proved difficult the world over.

In South Africa, the most recent national HIV survey revealed that 74% of those most at risk of acquiring the virus (including women aged 20–34) were unaware of their HIV status[5], even though their answers to survey questions indicated that they were well informed about the disease. In 2008, the United States Centers for Disease Control and Prevention (CDC) in Atlanta, Georgia, surveyed more than 8,000 men who have sex with men, and found that more than 40% of those infected did not know it[6]. Relatively few of those at risk who are uninfected are taking antiretroviral drugs as a preventive measure[7], which the CDC recommends.

The numbers volunteering for HIV tests paint a similar picture. Although testing has increased significantly in sub-Saharan Africa in recent years, only about 20% of men and 28% of women in South Africa received an HIV test and result within the past year. Similarly, in Kenya, the 2007 national AIDS survey of 18,000 individuals from nearly 10,000 households found that only 17% of those testing HIV positive reported knowing that they were infected[8]. China fares a little better: about 44% of people living with HIV know that they are infected[9].

Denial is not the only factor hampering HIV testing and the use of antiretroviral drugs. For instance, in South Africa the public health-care system is already overwhelmed by tens of thousands of AIDS patients. Long queues and overstretched staff discourage many from trying to obtain medical help. But in countries ranging from France to India the practical problems hampering testing and uptake of antiretrovirals are compounded by people seeking care only after they have developed the symptoms of full-blown AIDS.

Women attending an HIV clinic in Rwanda avoid the camera.

L.TOWELL/MAGNUM

We must not allow the fourth decade of the AIDS epidemic to be the decade of missed opportunity. Every prevention programme should involve a combination of interventions tailored to the risks and vulnerabilities of the people receiving them. In sub-Saharan Africa, for instance, teenage girls are up to eight times more likely to contract HIV than boys of the same age. For them, a microbicide gel that they can control is likely to be critical to reducing their risk of infection. Meanwhile, male circumcision is likely to have most impact for men in their early twenties.

The challenge is how to implement these strategies effectively with the limited funds available, so that the successes emerging from clinical trials translate into real-world benefits. The recent call by the CDC and the US National Institutes of Health for proposals for 'implementation science' programmes to address the global epidemic is a step in the right direction. Together, these agencies are committing about $50 million from PEPFAR to programmes involving interventions known to be effective in clinical trials, and which in combination are likely to improve HIV prevention, treatment and care in poor communities.

Most important, any programme of biomedical interventions should include strategies aimed at encouraging people to acknowledge their risk of contracting HIV.

WORKING TOGETHER

We cannot assume that demand for antiretroviral drugs, or for any other prevention technology, exists just because the need does. A government attempt to introduce female condoms in South Africa in 1995 illustrated the pitfalls of rolling something out without concomitantly creating a demand for it. The $2.6-million effort to distribute 1.3 million condoms to women proved ineffectual because patients did not request them and health-service providers did not adequately promote them.

South Africa's era of denialism at the highest political level illustrated that simply giving people facts and information is not enough. Fear and avoidance must be understood in the context of both the individual and society. Health practitioners and researchers worldwide must engage local communities to find out what factors are preventing people from making the best choices in terms of prevention and treatment. Community members and patients are best placed to advise practitioners how to couch advice and information in ways that are likely to be effective.

This approach has already proved successful in some cases. For instance, my co-workers and I designed a dosing strategy for the tenofovir microbicide gel whereby women apply one dose of gel within 12 hours before sex and a second as soon as possible within 12 hours after sex. We selected this strategy partly on the basis of scientific information about the drug and its effectiveness in animal studies — but also as a result of detailed consultations with rural women in South Africa revealing that having some flexibility over when to apply the gel was essential[10]. With this dosing approach, nearly 900 women enrolled in a clinical trial were able to successfully apply the gel about 80% of the time[2].

An underlying obstacle to finding effective ways to intervene is the separation between biomedical and behavioural research in HIV/AIDS. This emanates not only from our failure, as researchers, funders and clinicians, to fully appreciate that every biomedical prevention strategy includes a behavioural change, but also from counterproductive hierarchies and territorialism within science. If behavioural and biomedical scientists work together to develop solutions, the coming decade may prove to be the one when the tide was turned against the global AIDS epidemic. ■

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