

The other approach to tackle HIV persistence in patients taking ART is to lure HIV out of its hiding place in resting T cells. Activating latent virus might lead to death of the cell or make the virus ready for immune-mediated clearance. A range of licensed drugs that modify gene expression, including viral gene expression, are in clinical trials in HIV-infected patients on ART. Two studies^{8,9} have reported that HIV latency can be activated with the histone deacetylase inhibitor vorinostat.

There are now 15 HIV-cure-related trials being done worldwide.³ Clinical trials include investigations of increasingly potent histone deacetylase inhibitors, and of gene therapy to eliminate the CCR5 receptor from patient-derived cells.

HIV-cure-related trials raise many complex issues. Giving potentially toxic interventions to patients doing very well on ART needs careful assessment. At this early phase of research, participants will be unlikely to derive any direct benefits. Understanding risk-benefit, ethical issues, and the expectations and perspectives of the community will all be discussed and debated at IAS 2013 and the preceding IAS workshop, Towards an HIV Cure.

Developments towards a cure for HIV are exciting—for scientists, for clinicians, and most importantly, for patients. But we need to be realistic. Finding a cure will be a long and tough road, and will take many more years to achieve. We are at the very beginning, although many now believe that it might be possible to find a cure, at least for a small proportion of infected people.

We need to take inspiration from the many people who have delivered so much in the past 30 years, and continue to imagine, continue to innovate, and continue to work together towards an HIV cure—for everyone.

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Fighting the HIV epidemic in the Islamic world

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Early in the HIV/AIDS epidemic, most predominantly Muslim countries regarded HIV as a disease associated with sexual promiscuity, homosexuality, and drug and alcohol use—behaviours forbidden by Islam. Home to more than 1.6 billion Muslims, the Islamic world was widely believed to be somehow protected against HIV/AIDS. Adherence to Islamic beliefs, together with widespread practice of male circumcision, was thought to protect against the risk of HIV infection, and subsequently to account for a comparatively low HIV prevalence in Muslim majority countries in sub-Saharan Africa and the Middle East.^{1–3}

30 years into the epidemic, the reality is vastly different. HIV infection is a concern in several Muslim majority countries including Malaysia, Indonesia, and Iran, with prevalence rates in adults of 0.4%, 0.3%, and 0.2% in each of these countries, respectively.⁴ In most parts of the world, the HIV/AIDS epidemic has stabilised or decreased; however, of the nine countries where incidence rate has increased more than 25% since 2001, five—namely, Bangladesh, Indonesia, Guinea-Bissau, Kazakhstan, and Kyrgyzstan—have Muslim majorities.⁵ Furthermore, the number of people newly infected in the WHO Middle East and north Africa region has increased

by more than 35% (from 27 000 to 37 000).⁴ After the eastern Europe and central Asia region, the Middle East and north Africa region has the fastest growing HIV/AIDS epidemic in the world.

In many of these countries with predominantly Muslim populations, the HIV epidemic is characterised by being concentrated in high-risk populations, particularly people who inject drugs, female sex workers (FSW), and men who have sex with men (MSM)—practices forbidden by Islam. This has resulted in widespread stigmatisation and a reluctance to address the risks that exist within these communities. Implementation of evidence-based prevention programmes, such as needle-syringe programmes for people who inject drugs and provision of condoms for sex workers and their clients, has generally been met with resistance.

In Malaysia, only in 2005 when faced with an increasing HIV epidemic mainly driven by injection drug use did the government consent to implementation of harm reduction programmes, including needle-syringe and methadone maintenance programmes.⁶ Despite widespread public criticism, in particular from religious leaders, these programmes are now an accepted aspect of Malaysian public health policy and continue to be scaled up across the country. At the 2013 IAS meeting in Kuala Lumpur, Malaysia, data on the estimated number of HIV infections that have been averted following the implementation of harm reduction programmes will be presented.⁷

More broadly, this public health approach to drug use has had other important effects. Malaysia, which for many decades has relied on punitive actions against drug use including incarceration in drug detention centres, has additionally seen a gradual shift towards provision of voluntary treatment for drug use, including methadone maintenance therapy, through the establishment of Cure and Care Centres by the National Anti-Drug Agency.

Although harm reduction programmes for HIV prevention in people who use drugs has become acceptable in Malaysia, the same cannot be said for the adoption of evidence-based programmes among FSW, their clients, and MSM. HIV prevalence in Malaysia in FSW and MSM is not as high as that in drug users; an epidemiological survey in 2012 showed prevalence ranging from 0.7–18.5% and 2.0–13.7% in FSW and MSM, respectively, compared with 5.3–46.5% in people who inject drugs.⁸ By contrast to the strong political

and financial support for programme implementation provided by the Malaysian Government for harm reduction, programmes to address HIV infection in FSW and MSM have been greatly underfunded.

So how did harm reduction gain currency in countries such as Malaysia, Indonesia, and Iran, whereas programmes to address HIV among FSW and MSM continue to meet resistance? In these three countries, advocacy for harm reduction has centred not only on emphasising the extent of the HIV epidemic in people who use drugs, but has also focused on drug use and HIV/AIDS as a public health problem, and Islamic values about the preservation of life. These values must be protected and promoted in all circumstances, including prevention and treatment of any illness and disease.⁹ On the other hand, religious and cultural taboos against sex outside marriage, sex work, and homosexuality have made HIV prevention and treatment programmes largely impossible in Muslim majority countries, except Morocco and Lebanon for example.

In many Muslim countries strong moral views on HIV prevail including within the medical profession, giving rise to deeply rooted stigma and discrimination against people with HIV/AIDS and those perceived to be at high risk of infection.¹⁰ This prejudice forces the people most in need of HIV prevention and treatment programmes away from services. Many countries and policy makers are unable to separate the public health imperative of sound HIV prevention programmes, based on evidence, from private behaviour which is at odds with religious teachings.



AIDS awareness campaign in Malaysia

Nonetheless, there are signs that Muslim majority countries including those in the Middle East are beginning to address the HIV epidemic; many countries have recently developed national plans on HIV.¹¹ Parts of the Islamic world are also in the process of profound sociocultural transitions that are leading to increased tolerance and acceptance of practices such as premarital and extramarital sex.¹² What is often forgotten in the Islamic world's response to the HIV epidemic is that central in the teachings of Islam is the concept of compassion and justice. Muslims are encouraged to recite the phrase *Bismillah ir-rahman ir-rahim*, "In the name of Allah, most beneficent, most merciful", before undertaking any action—large or small.

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HIV pre-exposure prophylaxis in injecting drug users

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Globally, there are an estimated 15.9 million injecting drug users, 3 million of whom have HIV.¹ The illicit nature of injection drug use and associated social stigma have created substantial challenges for HIV prevention in this group. Despite these obstacles, several programmes have shown that HIV transmission in injecting drug users can be prevented, stabilised, and even reversed with needle exchange programmes.² However, the HIV epidemic continues to grow in this high-risk population in some regions, particularly in eastern Europe, central Asia, and, since 2007, sub-Saharan Africa.³ Much more needs to be done to reduce the continuing high rates of HIV transmission in injecting drug users.

Findings from a series of randomised placebo-controlled trials, viewed cumulatively, provide compelling evidence (figure) that antiretroviral pre-exposure prophylaxis (PrEP), when taken, is effective in preventing mother-to-child transmission of HIV,⁴ sexual transmission in men who have sex with men, and sexual transmission between men and women.⁵ In women, both oral and topical antiretrovirals have been shown to prevent sexual transmission. However, there is no rigorous evidence on

whether PrEP is effective in preventing parenteral HIV transmission. In 2005, the US Centers for Disease Control and Prevention initiated the Bangkok Tenofovir Study to address this major gap and assess the efficacy of daily oral tenofovir disoproxil fumarate (tenofovir) in preventing parenteral transmission of HIV.

In *The Lancet*, Kachit Choopanya and colleagues report the results of this important study.⁶ They enrolled 2413 participants who reported injecting drugs within the previous 12 months and followed them up for a mean of 4.0 years. During follow-up, 50 participants acquired HIV: 17 were in the tenofovir group (HIV incidence=0.35 per 100 person-years) and 33 were in the placebo group (0.68 per 100 person-years), which translates into 49% effectiveness of tenofovir (95% CI 9.6–72.2). Additional per-protocol and drug level analyses drew attention to the importance of adherence to achieve high levels of protection from PrEP.

Although findings from this study provide the evidence to show that PrEP is effective in preventing HIV infection in people who inject drugs, it is less clear as to whether the findings show that PrEP prevents parenteral