

## The 16<sup>th</sup> International AIDS Conference, Toronto, 2006 Working to Increase the Response to the Growing Global Epidemic

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The 16<sup>th</sup> international AIDS conference was held in Toronto from August 13–18, 2006, with approximately 20 000 participants making it the largest ever. Over 38 million persons are living with HIV while 4.1 million people were newly HIV infected and 2.8 million died during 2005 (1). Sub-Saharan Africa continues to be most affected with 24.5 million persons living with HIV/AIDS. The epidemic continues to grow in South Africa and India, among injection drug users (IDU) in Eastern Europe, among IDU and men who have sex with men (MSM) in South East Asia and among young black MSM in the United States of America (USA). There are many hidden HIV epidemics affecting marginalized groups including mobile populations, refugees and internally displaced persons. Pre-existing stigma associated with vulnerable and marginalized groups is aggravated by HIV related stigma, which continues to drive the HIV/AIDS epidemic. Structural factors, gender inequity and infringement of rights all contribute to increased social vulnerability and spread of HIV. Although developed countries and a small number of developing countries have made definite progress in controlling their epidemics, 25 years after the first report of AIDS in 1981, the HIV/AIDS pandemic continues to outstrip the response.

At the conference, there was an encouraging recognition of the need to prevent new HIV infections. Prevention services are simply not reaching millions of persons in need (2, 3). Less than 10% of pregnant women globally are given anti-retroviral (ARV) drugs to prevent HIV transmission to their newborn infants (1). Hence 14% of all new HIV infections, most of which are fully preventable, are among children. Fifty per cent of young people do not have basic information on HIV and how to prevent it, while condoms are accessible to only 21% of sexually active persons. Prevention services for vulnerable populations are estimated to reach only 16% of sex workers, 11% of MSM and less than 10% of IDUs.

The need to increase access to prevention services based on evidence was stressed. Although most studies show that abstinence-only programmes for youth do not work,

there was one report of a successful abstinence-only intervention (4). The evidence does support sex education programmes, access to condoms and voluntary counselling and HIV testing (5–8). Harm reduction (education, clean syringes and drug substitution with methadone or buprenorphine) for IDU significantly reduces new HIV infections and is safe and cost-effective (9, 10). Injection drug users now accounts for 10% of all new HIV infections. It is unfortunate that the USA Government continues to oppose harm reduction programmes and to impose conditions on the use of their funding for AIDS control.

An effective HIV prevention vaccine is the best option for controlling the HIV/AIDS epidemic in the long term (11). There are a number of HIV vaccine candidates in trials and a variety of new concepts for vaccines in development. However, it is unlikely that there will be an effective HIV vaccine in the near future due to the numerous challenges faced. HIV shows great genetic diversity and infects both the immune defense cells as well as the antigen presenting cells. It spreads rapidly from cell to cell, integrates into the genome and resides in the memory cells. Traditional approaches have aimed to stimulate neutralizing antibodies and T-cell lymphocyte responses. Future HIV vaccine strategies may need to be based on novel and creative vaccine concepts.

Much more research is now being done with microbicides using a variety of different approaches (12). There are currently five products in large-scale efficacy trials and another 14 in early trials. The first generation of microbicides include acid buffer gels and entry inhibitors while second generation products include the use of ARVs such as tenofovir and the nucleoside reverse transcription inhibitors (NRTI). An effective microbicide would provide women with a method over which they have full control. This is critical due to widespread gender inequity and the difficulty many women have in negotiating safe sex. There were calls by MSM for a similar product to be developed for their use.

Based on ecologic and observational studies and one randomized controlled trial (RCT) male circumcision appears to reduce the risk of HIV infection (13–15). Two other RCTs are underway. If the protective effect of male circumcision is confirmed, the challenge will be how to make this surgical procedure widely available in a safe and cost effective way. Most experts agree that the treatment of sexually transmitted infections contribute to HIV control although only one of four RCTs has clearly established this to

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be the case (16–18). Trials are now underway to test whether suppressive treatment of *Herpes simplex* virus will reduce the risk of HIV infection. Post-exposure prophylaxis with ARV therapy following needle stick injury is well established (19). Pre-exposure prophylaxis with a daily dose of tenofovir or tenofovir and emtricitabine is being studied. All these approaches offer the promise of additional options for prevention. They are well described in a publication by the Global HIV Prevention Working Group titled ‘New approaches to HIV prevention; accelerating research and ensuring future access’ that was launched during the conference (20). While everyone welcomed the research into new preventive options, there was considerable concern over the failure to make current methods of HIV prevention more widely available.

Access to ARV treatment is also lagging far behind in most developing countries despite the campaign led by the World Health Organization (WHO) to place three million persons living with AIDS on ARV treatment by 2005 (21). Only 20% of persons living with HIV/AIDS (PLWHA) globally are on ARV therapy (1). A meta-analysis showed that adherence to ARV in Africa was better than in North America (77% compared with 55%) (22). This remarkable finding puts to rest the voices in the developed world that ARV could not be rolled out in resource poor settings. However, building sustainable health capacity is a major challenge for many developing countries. For instance, Africa may lose 30% of its health workers in the next 10 years due to AIDS and migration. The World Health Organization has launched a train, retain and treat initiative to address this need. Another important challenge is to reduce the high burden of morbidity and mortality due to tuberculosis among PLWHA. Much more needs to be done to scale up tuberculosis programmes with increased access to ARV therapy (23).

There continues to be important developments in ARV therapy with new products and formulations. The first once daily triple therapy pill is now available (Atripla: tenofovir, emtricitabine and efavirenz). A twice-daily formulation of stavudine, lamivudine and nevirapine has been available for some time and is used widely in Africa. The formulation of lopinavir/ritonavir (Kaletra) has been improved to two heat stable tablets twice daily. Two new potent protease inhibitors are now available namely triconavir and darunavir. It is generally accepted that protease inhibitors should be boosted with ritonavir. Other ARV drug products are being developed and there were encouraging reports of an integrase inhibitor.

The new WHO ARV treatment guidelines are more consistent with other recognized guidelines and recommend the need to consider the initiation of treatment in asymptomatic patients with a CD4 count below 350 cells (24). The approach to first line ARV treatment remains the same. However, there will be an increasing challenge for countries to provide the more costly second line drugs for patients

failing first line regimens. The role of resistance testing is increasing in managing patients on ARV therapy though it is expensive and unavailable in most of the developing world. The need to achieve fully suppressive treatment, defined as plasma HIV RNA of less than 50 copies, was stressed. Full adherence to ARV treatment remains critical to avoid early development of HIV resistance and treatment failure. Structured treatment interruption is generally not recommended because of early viral rebound (25). There are now data to show that clinical end points are predicted by baseline CD4 count, change in viral load and CD4 count at 24 weeks. Micronutrient supplementation appears to increase CD4 counts in PLWHA on ARV therapy (26).

As more patients are placed on ARV therapy, the question arises whether HIV transmission may be reduced due to the decrease in viral load in PLWHA. It has been shown that HIV transmission is related to viral load in HIV discordant couples and pregnant women (27, 28). If this is the case, increasing access to ARV treatment will contribute to prevention (29). At the same time there is a concern that ARV treatment could contribute to disinhibition or increased risk behaviour among persons living with HIV. Among children with AIDS, much more must be done to put them on ARV treatment. In developing countries, 25% of children with AIDS die within one year and 50% by two years of age. If the mother survives, the death rate among the children is halved. Co-trimoxazole reduces mortality among children with AIDS by 43% while malnutrition increases the risk of death five-fold. The growing number of AIDS orphans is another important challenge. For the first time, grandmothers who are playing a critical role in their care, were well represented at the conference.

The need to increase HIV testing as an entry point for treatment and prevention was stressed at the conference. Increasing numbers of AIDS experts are in favour of routine opt out approaches to HIV testing, though some raised concerns about possible infringements of human rights. There are clear advantages to knowing one’s HIV status. Persons testing negative can strive to reduce risky behaviour and practice safe sex in order to maintain their HIV free status. Persons testing positive can access treatment before they become ill and take steps to avoid infecting their sexual partners. However, given the continued stigma associated with HIV and the discrimination against persons with HIV/AIDS, there is an additional responsibility to ensure that efforts to increase HIV testing are accompanied by measures to respect the rights and autonomy of individuals as well as preserve their privacy and confidentiality. Unfortunately, many PLWHA do not inform their sexual partners of their HIV positive status. It is recognized that more has to be done with persons living with HIV to promote prevention and disclosure to partners.

Advances in molecular biology were shared at the conference including the role of cytokines in the immune

response and viral characteristics associated with HIV fitness and disease progression. Apparently HIV uses a decoy RNA to suppress the host cells' RNA defense mechanism. Note was made of 'elite' HIV survivors who have lived for 15 years without signs of progression to AIDS as well as sex workers who are repeatedly exposed to HIV without becoming infected. These persons are the attention of research so that HIV pathogenesis and host immunity could be better understood.

Political leadership is essential to ensure that scientific advances are translated into effective public health action. Political leaders have endorsed the UNGASS AIDS declaration (the political statement of commitment at the 2<sup>nd</sup> United Nations General Assembly Special Session on AIDS, July 2006) including setting goals towards achieving universal access to HIV prevention, treatment and care. The truth is that the rhetoric of most political leaders on HIV/AIDS far outstrips their action. President Mbeki of South Africa and his Health Minister were criticized also for their inept response to their massive HIV/AIDS epidemic in which 30% of pregnant women are HIV positive. It was reassuring to note the presence and participation of Prime Minister Denzil Douglas of St Kitts who has responsibility for health within CARICOM. Former US president Bill Clinton was visible and articulate alongside Bill and Melinda Gates and celebrity actor Richard Gere. The Gates foundation has contributed considerable sums for AIDS research and programmes. Stephen Lewis, UN ambassador for AIDS in Africa, gave a hard hitting address at the closing session calling on G8 leaders to live up to their commitments to provide funds for AIDS.

The Caribbean was well represented at the Toronto meeting with nearly 100 delegates, several oral presentations, posters and abstracts as well as a PANCAP satellite session and exhibition booth. Kerrel McKay, youth advocate from Jamaica, spoke at a plenary session while Penelope Campbell, UNICEF Jamaica, won a young researcher prize for her study among youth using the 'Bashy bus' (30). The Caribbean can definitely achieve universal access to HIV prevention, treatment and care provided we strengthen our leadership and coordination at both national and regional levels, show greater resolve and tackle the sensitive social issues that impede a more effective response to the HIV/AIDS epidemic (31).

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