Canadian Association for HIV Research | 23rd Annual Canadian Conference on HIV/AIDS Research • Highlights

CAHR 2014 NEWSLETTER

In This Issue

Mark Wainberg Lecture

Science and Human Rights Should Inform Public Policy

Richard Elliott

In this year's opening lecture, Richard Elliott, Executive Director of the Canadian HIV/AIDS Legal Network, stressed the need for scientific evidence and human rights to be given precedence over politics and bias in the shaping of law and public policy relating to HIV and AIDS. While countries such as Russia and Uganda have recently made headlines for their rancorous anti-homosexual policies, Elliott contended that the Canadian government has also taken positions that run contrary to scientific evidence and negatively affect human rights among people who have or are at risk of acquiring HIV.

Evolution of the Response to HIV

The federal government response to HIV/AIDS has gone through several stages since the epidemic began more than three decades ago. In the early 1980s, AIDS was "largely seen as a concern of the marginal," he said. Interest and concern increased once the disease had felled celebrities such as Rock Hudson, HIV was identified as the source, and blood testing became possible. In this second phase, government commitments to battling AIDS, while often ad hoc, were initiated.

A third phase, in the late 1980s, was marked by community activism and calls for governments to develop coherent action plans against the disease. It was during this period that the first Canadian AIDS strategy was adopted and the response to HIV was framed, at least in part, as one of human rights.

By the fourth phase in the late 1990s, Mr. Elliott noted, "some of the urgency in AIDS activism had been lost in many quarters, including government, which is such a key player in mobilizing a national response." Ralf Jürgens, a former executive director of the Legal Network, described the federal strategy of the time as "government administering the epidemic." Even as infections spread and the epidemic became demographically and medically more complex, the government's funding commitment remained fixed.

The current fifth phase dates roughly from the release in 2005 of the latest Canadian HIV action plan, Leading Together. "It represented what could and should have been a significant development… It was explicitly grounded in evidence and guided by human rights and social justice principles," Mr. Elliott remarked. However, he added, there was little evidence the program was actually supported by the federal

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Vaccine Research Plenary

HIV – Progress in Combination Prevention

Dr. Catherine Hankins

In the past five years, a number of new strategies for preventing HIV acquisition and transmission have been identified. Such efforts are especially important given the ongoing challenges in developing one or more effective vaccines against the virus. If deployed effectively, combination prevention can likely have a substantial impact both for individuals and on a population level.

The need for multipronged HIV prevention is emphasized by current statistics from the World Health Organization. As of 2012, 35 million people were infected with the virus. Although the incidence of infection has decreased by 33% since 2001, some 2.3 million new cases occur every year, observed Dr. Catherine Hankins, Deputy Director, Science, at the (University of) Amsterdam Global Institute for Health and Development. Some 10 million individuals in low- and middle-income countries undergo antiretroviral therapy (ART). With new guidelines in place suggesting treatment should be initiated when a patient's CD4 cell count reaches 500/microlitre, ART coverage is only about 34%.

Figure 1) Dr Hankins summarizes HIV prevention

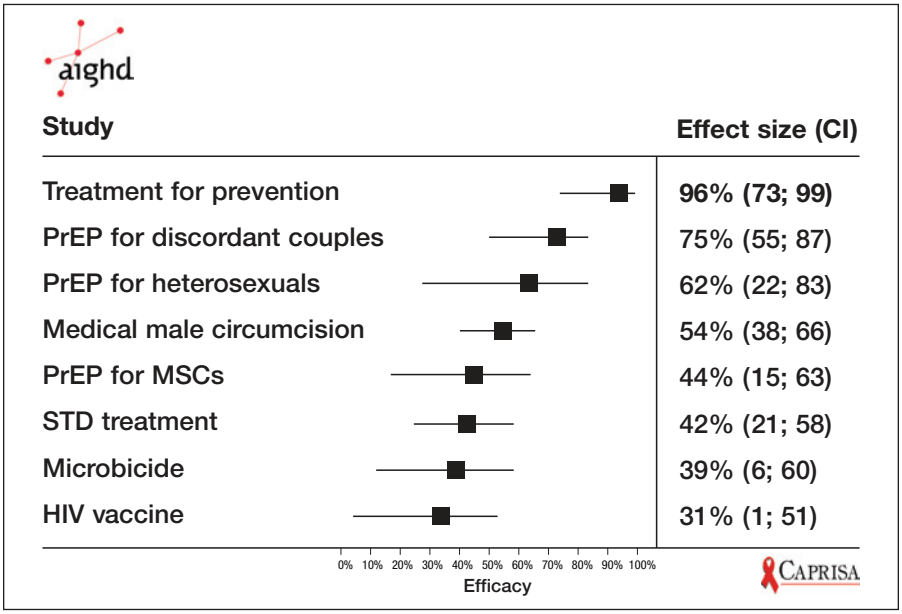


Figure 2) Clinical trial evidence: Prevention of sexual HIV transmission

Biomedical, Behavioural, Structural

Combination prevention is defined as a strategy that puts together biomedical therapies, behavioural interventions and structural elements "to address the immediate risks, the underlying vulnerabilities and the pathways that link them," Dr. Hankins stated.

There is no single best or "cookie-cutter" combination approach. Combination prevention must be "evidence-informed, human rights-based and context specific… tailored to local epidemics and needs... It adapts to changing epidemic patterns and rapidly deploys new innovations. It's very dynamic," she continued. Decentralized administration and community engagement are crucial. "You don't just tell people what to do, expecting them to do it. We look at social context, social norms, what is the enabling environment that needs to be put in place to make it easy for people to make the right choice."

Dr. Hankins summarized the range of prevention methods now available. Figure 2 indicates the efficacy of some of these documented in clinical trials.

One non-drug option for which policies and programs have been established in various regions is medical male circumcision (MMC). The number of MMCs needed to prevent one infection varies (countries with high incidence and prevalence derive the greatest benefit) but is less than 10 in several countries, Dr. Hankins indicated. Zimbabwe, for example, will be able to avert more than 40% of infections with 80% MMC coverage. The greatest impact would be expected in South Africa. Although the worldwide cost to ensure 20 million MMC procedures is significant, at $1.5 billion, the resulting savings in averted ART costs is more than 10 times that amount, she noted. Several innovations have been developed to reduce costs, including the use of surgical glue to avoid sutures and devices that permit the procedure to be done rapidly and without the need for follow-up visits.

Treatment as Prevention

In recent years studies have demonstrated the efficacy of ART in preventing onward transmission of HIV. As treatment is scaled up, there is a population benefit from the lower community viral load, Dr. Hankins said. "When you get to 30% to 40% ART coverage among people living with HIV in

your community, HIV acquisition hazard can be reduced by 38% – around a 1.4% decrease for each 1% increase in ART. This is striking."

In the HPTN052 study of serodiscordant couples, early treatment led to a 96% reduction in HIV acquisition. "That level of impact is just phenomenal," Dr Hankins commented. However, ART therapy is seldom initiated at the levels used in the HPTN052 study. A recent report by Egger et al indicated the median CD4 cell count at start of therapy was below 200 in low- and middle-income countries, versus 300 in higher-income countries, Dr. Hankins said. Furthermore, while in the US some 28% of patients on treatment are virally suppressed, the percentage in West Africa is closer to 10%. "So we have a lot to do to make treatment be a major contributor to HIV transmission reduction."

In a test-and-treat strategy, ART is offered upon HIV infection diagnosis regardless of the CD4 cell count. "This is particularly important for people likely to be lost in the treatment cascade [when] there's no point in telling them to come back in three or six months. Now is the time to start talking to them about treatment and getting them started." However, to deploy this strategy far more HIV testing needs to be performed and links to treatment services strengthened, Dr. Hankins stated.

Pre-Exposure ART

Various forms of ARV therapy have been shown to be effective for pre-exposure prophylaxis for HIV-negative sexual partners, so long as adherence is maintained (Figure 3). Trials under way, including IPERGAY and ADAPT, will help ascertain whether intermittent PrEP is effective in MSM. NEXT-PREP is evaluating the role of maraviroc in the same population. For women, preparations currently being investigated include long-acting injectable forms of rilpivirine and the integrase inhibitor GSK744; and an intravaginal ring containing dapirivine that is replaced once a month.

Because adherence to PrEP regimens has sometimes been poor, it will be important to conduct further research in this area and for health care practitioners and patients to discuss what will work best for each person and situation. Moreover, the agent must be selected for efficacy in the appropriate tissues. For example, oral tenofovir/emtricitabine exhibits 100-fold higher concentrations in rectal than cervicovaginal tissue. The gel version of the same drug achieves 1000-fold higher concentration in the vaginal tissues than does the oral medication. "The right time, right population, right timing, right delivery, right decision making" are all important, Dr. Hankins stressed.

In addition, as more data on PrEP efficacy emerges, it will be important to define when it should become part of the standard of prevention offered to all arms of a prevention trial, she observed.

aighd	% of blood samples with tenofovir detected	HIV protection efficacy in randomized comparison	HIV protection estimate with high adherence
Partners PrEP	81%	75%	90%
TDF2	79%	62%	78%
BTS	67%	49%	70% – 84%
iPrEx	51%	44%	92%
FEM-PrEP & VOICE	<30%	No HIV protection	N/A

Less than 50% of participants assigned to active product in the VOICE C substudy (similar to VOICE overall), had drug on board despite 97% study retention.
(van Stratan, AIDS Impact 2013)

Figure 3) Adherence is important for protection

Clinical Sciences Plenary

HIV-HCV Coinfection: Current Picture and Glimpse of the Future

Dr. Marina Klein

Operating since 2003, the Canadian Coinfection Cohort (CCC) study has enrolled more than 1200 patients in 19 centres and has accumulated some 4000 person-years of follow-up. The substudies conducted under the CCC umbrella have created a comprehensive prospective database with details on sociodemographics, drug/alcohol use, treatment status, and outcomes among a representative sample of Canadian individuals infected with HIV and hepatitis C virus (HCV). Its findings to date and concepts for further research can potentially help optimize the use of new HCV therapies in this population, according to Dr Marina Klein, Professor of Medicine, Chronic Viral Illness Service, McGill University Health Centre, Montreal.

"The simultaneous development of multiple curative therapies for hepatitis C is unprecedented in modern infectious disease," she remarked. Nevertheless, making a dent in the HCV epidemic will require improving access to therapy for patients in this clinically challenging coinfected population.

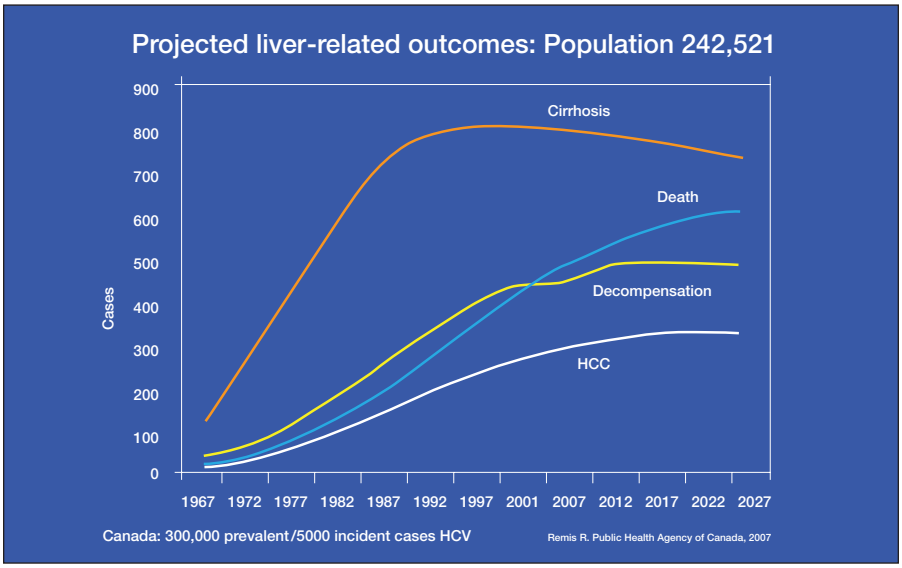


Figure 1) Projected liver-related outcomes

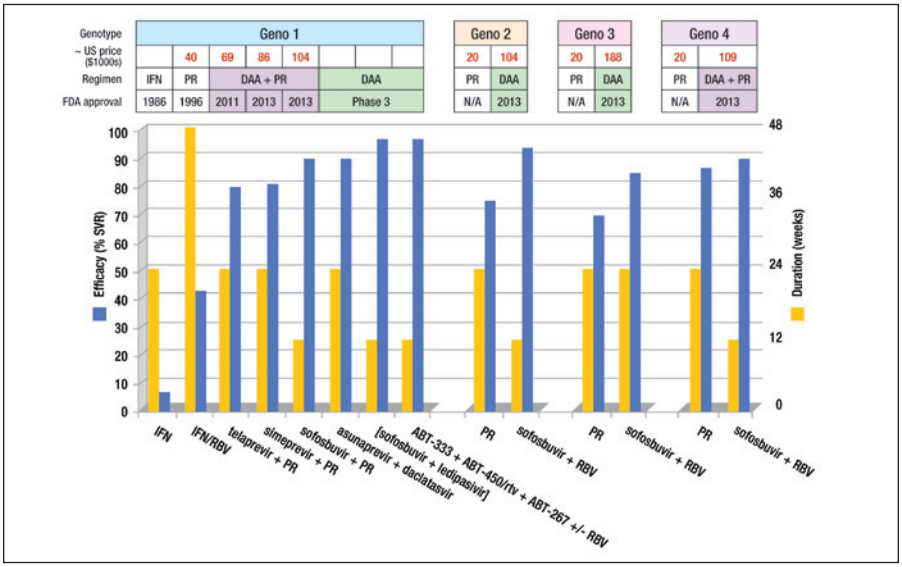


Figure 2) SVR rates with HCV therapies

Profile of Coinfection

In Canada, at least half of HCV cases can be traced to the use of injected drugs. Eight out of 10 CCC participants have injected drugs; 35% report continued use. Sexual exposure (~10% of cases in 2013) principally occurs among men who have sex with men (MSM). Although nearly 80% of the CCC participants are white, Aboriginal individuals (who account for about 3% of the Canadian population) make up a disproportionate 16%. Genotype 1 accounts for more than 70% of cases.

About one in five CCC participants had undergone treatment for HCV (most often with pegylated interferon/ribavirin) as of their enrolment; 35% had been treated as of their last clinic visit. Two-thirds of these have not responded to treatment. "So [with] the 'glass half empty' perspective, we see that almost 75% of our participants still have active hepatitis C replication," said Dr Klein. As such, they remain at risk for liver disease and other complications of HCV. Their status is reflected in the very high mortality rates observed. Overall, participants are 12 times more likely to die prematurely than age-matched Canadians. Women are 20 times more likely to die subsequent to HIV/HCV coinfection.

About 20% of deaths result from end-stage liver disease. This is unsurprising, noted Dr Klein, given the course of HCV. As shown in Figure 1, adverse outcomes related to the start of the epidemic are starting to peak. "We are now at that time – with the bulk of the epidemic having started in the 1960s and 70s and 80s – [at which] we can expect to see large numbers of liver-related events, out probably to 2030… Hopefully, these curves than be dramatically modified by the introduction of curative hepatitis C therapy but that remains to be seen."

A significant proportion of mortality in CCC participants (18%) is due to drug overdose, Dr Klein added. "We are still not doing enough with respect to harm reduction."

HIV/AIDS accounts for only about 5% of deaths, suggesting, she remarked, that "effective HIV treatment is possible even among patients who often have difficulties with adherence and are marginalized… That should be good news, going forward."

Effects of Antiviral Therapies

Among the complexities of treating HIV/HCV coinfection is that antiviral therapy for one virus can have a negative impact on the other illness. For example, CCC researchers have determined that liver fibrosis progression may be enhanced by boosted protease inhibition. Possible causes are metabolic changes or hepatic steatosis resulting from cumulative toxicity, Dr Klein indicated. This finding corresponds with data showing that coinfected patients whose HIV is fully suppressed have a two-fold higher risk of hepatic decompensation than those with HCV monoinfection.

Other work has shown that HCV coinfection negatively affects immune reconstitution after initiation of antiretroviral therapy (ART) for HIV. Insulin resistance, which increases the risk of liver fibrosis, has increasingly been recognized as an issue in CCC participants, and may be the result of either HCV itself or ART.

Aiming for Cure

It is necessary to target HCV as well as HIV in the coinfected patient, Dr Klein stressed. "It's clear that hepatitis C treatment is what we need to be able to bring to the population to be able to improve health at a broad range of levels." Fortunately, it is possible to achieve a cure or sustained virologic response (SVR) with current and emerging therapeutic regimens. Ideally, the daunting complexity and side effect profiles of standard treatments, which have limited their application in coinfected patients, will be alleviated with the newest direct antiviral agents (DAAs). "The interferon-sparing DAAs have tremendous potential to improve things for this population," she noted. Cure rates approaching 100% have been achieved with regimens of eight to twelve weeks' duration, as compared with 70% to 80% with a 24-week course of pegylated interferon/ribavirin (Figure 2).

"SVR leads to improvements in a variety of outcomes in coinfection, including overall mortality, liver-related mortality, hepatic decompensation and… maybe even hepatocellular carcinoma," Dr Klein summarized. Furthermore, following treatment for HCV, patients report better quality of life. In the CCC population, "[the] 10 points on the EQ5D scale was considered clinically meaningful, akin to what you might see in patients who receive cancer chemotherapy and achieve remission. So probably important." Health care utilization among achievers of SVR is also lower (for example, an 80% reduction in inpatient visits), "so this speaks to the potential for an important impact on health economic outcomes."

Challenges

The biggest stumbling block to wider use of new HCV therapies is their substantially higher cost than pegylated interferon/ribavirin, Dr Klein noted. If their costs remain elevated, health care funding agencies may restrict them to the HCV genotypes that have been most difficult to treat, she suggested.

Access to treatment for coinfected patients is not easy, she added. Patient-related factors include low socioeconomic status and marginalization, ongoing substance abuse, decompensated liver disease, poor awareness or education about their illness and therapy, and risk of side effects and drug interactions. In the CCC, women, Aboriginal people and patients with a history of crack or cocaine use were least likely to receive treatment. Despite the existence of treatment guidelines, physicians' opinions and perceptions about a patient's eligibility also play a role. "Two factors consistently rated as important were severity of fibrosis and current alcohol intake," Dr Klein reported.

A cautionary finding in the CCC is that many patients resumed or even increased alcohol use after achieving SVR. "We have to be cognizant of this because these patients still have fibrosis and they could still be at risk for developing liver outcomes related to alcohol. I think harm reduction following treatment is going to be very important," Dr. Klein observed. Similarly, reinfection rates after cure remain very high. "This is going to be an issue that needs to be figured in the mix," she added.

Further Questions

Among areas to be addressed in future CCC endeavours include the best models and approaches for use of DAAs in coinfected patients, Dr Klein stated. To date, trials of DAAs have enrolled only "ideal" populations, so "observational studies are going to continue to have a very important role in conducting real-world evaluations of these therapies... The comprehensive data on the real-life impact of these therapies that we will gather will be essential to determine how to best treat coinfected patients, and be critical to help us individualize care and prioritize treatment decisions and in guiding allocation of resources."

Turning the Tide on HIV

The 23rd Annual Canadian Conference on HIV/AIDS Research – CAHR 2014 – was held May 1–4, 2014 in St. John's, Newfoundland and was co-chaired by Drs. Michael Grant and Debbie Kelly from Memorial University. With the 2014 theme of *"Turning the Tide on HIV"*, CAHR had a stellar program of world-renowned speakers, allowing participants to connect with researchers, frontline public health and community-based workers, policy makers, people living with HIV and AIDS, and others interested in the field of HIV research.

Social Sciences Plenary

The Case for Social Sciences in HIV Research

Dr. Richard Parker

Investigations into the prevention of HIV have recently focused on biomedical strategies. Nevertheless, a review of the history of the HIV/AIDS epidemic shows that social sciences are vital to comprehensive research, said Dr Richard Parker, Professor of Sociomedical Sciences and Anthropology at Columbia University, New York. "Social science is absolutely crucial to most fundamental questions we are asking about the epidemic and that we need to try to confront," he remarked.

Lessons from History

Table 1 lists the evolving paradigms in HIV prevention. The earliest responses to HIV were led by the communities most affected by it, Dr Parker recounted. Developments he described as "the art of caring" and "the construction of solidarity" continue to characterize community approaches today. "Cultural activism [and] cultural mobilization, in a time when biomedicine and public health offered next to nothing in terms of how to respond to the epidemic, were profoundly important and continue to be an underlying principle of the response to HIV since that time," he commented.

By the 1990s, researchers around the world had mobilized to develop theories, investigations, and methods that could be used to assist HIV prevention. "A new wave of approaches, which I describe as behavioural theories and interventions, began to be rolled out around the world," Dr Parker said. Cognitive behavioural approaches initiated in the US were dominant in research during that period. Social science studies played a key role in this phase by pointing out inhibitors to suggested modes of HIV prevention such as social, political, economic and gender inequalities. "Even though behavioural models and interventions have continued to be important parts of the field on up to the present, by the [1990s] we had become aware of the limitations of those kinds of approaches – of the difficulties that they confronted when they came in contact with the reality of structures and cultures around the world."

Similarly, with the development of effective antiretroviral therapies, a focus by social scientists on structural barriers was important to a discussion of access to treatment. This discussion continues today, Dr Parker reminded the audience. In some ways, he noted, "there has been only limited change in most of the important structures that shape the epidemic. Whether that's economic exclusion or gender inequality or what have you… Policies and politics may both shape risk and vulnerability more than anything else. The kinds of political silences and irresponsibilities in the first decade of the epidemic that have continued in many parts of the world on up to the present may actually be the biggest structural barrier [to an effective response to HIV]."

Biomedical Focus

Against this background, it is not surprising that the research pendulum has swung back toward biomedical strategies, observed Dr Parker. "[We seek] not necessarily just the magic biomedical bullet but a range of biomedical solutions that would perhaps enable the response to HIV/AIDS to escape the difficulty of overcoming structural barriers that are so hard to change." Again, social science researchers can play a key role by helping to ascertain which of the numerous biomedical strategies can be used most effectively, and how, he indicated. Appropriate application of biomedical prevention requires social investigation and analysis, including research on the organization of health services and the economic and political landscape of service delivery, he noted.

Table 1
Paradigms in HIV Prevention

- Community based (culturally meaningful) prevention approaches and responses
- Behavioural theories/interventions
- Structural factors/interventions
- Biomedical prevention
- Combination prevention

For example, as HIV specialists study and/or promote pre- and post-exposure prophylaxis with medications, it is "an extremely high priority that we need to continue to investigate the social dimensions because it is not simply 'taking a pill'." Similarly, promotion of medical male circumcision has culturally mediated limitations in many parts of the world, and these need to be considered.

Combination prevention strategies also face barriers, "almost all from the complicated middle ground between individual behavior and structure," and these require significant investigation and critical thought, said Dr Parker.

"Social sciences will have to continue to be not just the handmaiden of other forms of HIV research but a fundamental partner of other kinds of research, to be able to respond to the epidemic even in an era of biomedical prevention that we hope will prove to be more effective than other approaches." Social sciences also produce narratives that are as important as data, because they provide a human face and cultural or community perspective and meaning to the numbers produced, he remarked.

Basic Sciences Plenary

Seeking Tools for Eradication of Infection

Dr. David Margolis

Interest in eradication of HIV infection has been rekindled, noted Dr David Margolis, Professor of Medicine, Microbiology, Immunology and Epidemiology at the University of North Carolina, Chapel Hill and Director of the Collaboratory of AIDS Researchers for Eradication (CARE).

While significant advances have been made with current antiretroviral regimens as both treatment and prevention, these cannot extinguish the infection. If therapy stops, latently infected cells have the capacity to reignite replication and spread infection. "We need to reduce the worldwide population of people that are HIV-infected… We need a back door to get out of treatment for millions of people for decades and decades," Dr Margolis asserted. Nevertheless, there remain major hurdles to overcome in the development of HIV-clearing agents.

A Viral Reservoir

Numerous cell types have the potential to contain replication-competent virus. However, among these, only resting CD4+ T-cells have been definitively identified a reservoir of latent HIV. "Then there's the ongoing debate about whether enough drug gets to every nook and cranny of the body all the time to prevent new replication," added Dr Margolis.

The generation of latency is probably the result of transcriptional silencing during memory cell differentiation, he explained. It is likely part of the normal biology of T cells which, in response to an antigen, expand and proliferate. Most of these cells manufacture virus and then die. Some revert to the resting state to create immunological memory, thus trapping the virus (Figure 1). As shown in Figure 2, a stable population of infected T-cells can be harvested from patients with durable HIV suppression. "It would take decades and decades of therapy for this reservoir to decay on its own. Basically, that's impractical," Dr Margolis indicated.

One challenge in targeting latent virus is that infection in resting CD4+ cells is difficult to detect outside highly specialized research laboratories. It does not correlate well with HIV DNA or RNA. Some data suggest that in patients with very large reservoirs of latency, HIV RNA may sometimes be detectable even when T cell counts are lower than 50 copies/microliter. Because this is not always the case, however, low-level viremia cannot be used to follow latency over time. At present, the best method for measuring latency is a viral outgrowth assay that is both time consuming and complex.

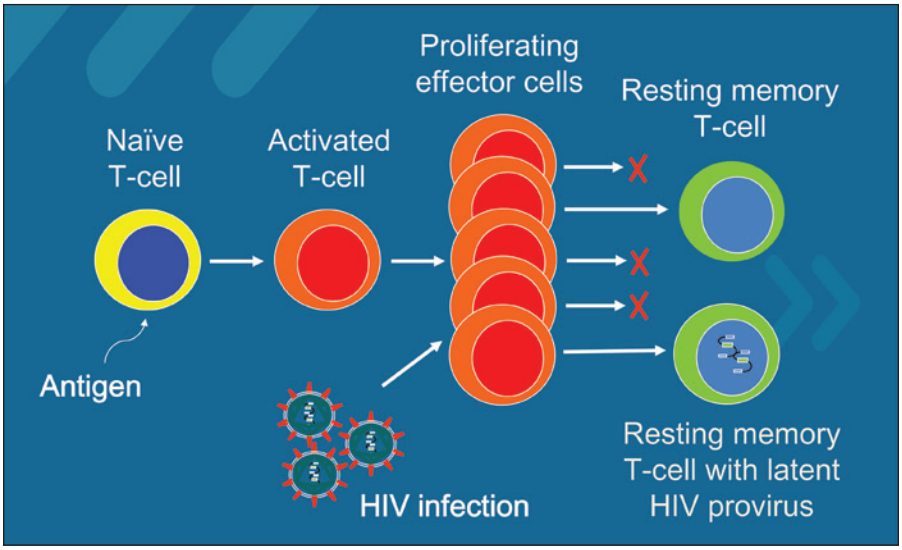


Figure 1) Generation of latently infected cells

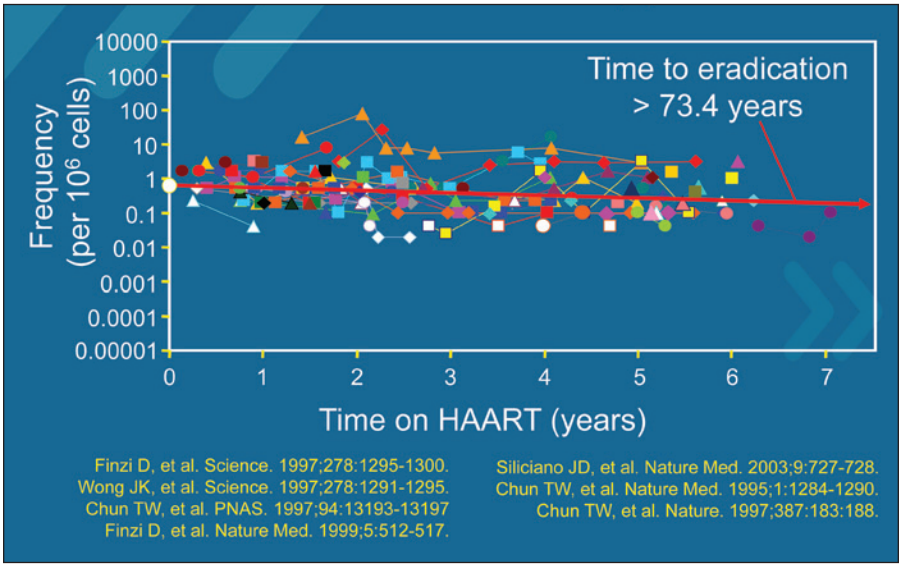


Figure 2) Latent HIV infection persists despite antiretroviral therapy

Targeting Latency

Latently infected cells are invisible to the immune system and present a poor drug target because they do not manufacture antigen and produce very little viral RNA.

A first research step is to seek ways to make the cells visible. "Then we probably need a second step to help clear [kill] the infected cells more effectively," Dr Margolis explained.

As such, the putative targets in a latently infected cell are the molecular mechanisms that control its "on-off" switch. One such target is histone acetylation. "A simple way to think of it is to think of the deacetylated, so-called tightly wound chromatin as turned 'off', and the acetylated chromatin as turned 'on'," Dr Margolis said. Numerous investigators have demonstrated that the deacetylated state correlates with latency, and that acetylating histones around the HIV genome allow the virus to be expressed, he said. Agents known as HDAC inhibitors block the deacetylation of chromatin. In three studies, a single dose of an HDAC inhibitor

(vorinostat or SAHA) induced enough viral expression from latent cells (especially in the presence of a large reservoir) to produce measurable HIV RNA. Figure 3 shows HIV RNA in 8 patients before and after the treatment.

Eradication of HIV will require repeated induction, which may be problematic. Dr Margolis's team has shown that when an HDAC inhibitor was administered three times a week, histone acetylation was increased 1.7-fold with the first dose but changed little afterward and "after dose 11 and 22 we saw almost no indication of HIV RNA." The investigators hypothesized that acetylation needs to be "reset" in the cells before they can respond to another dose of antilatency agent. As such, an optimal dosing schedule remains to be established.

Moreover, it appears that each episode of induction with the HDAC inhibitor vorinostat flushes out only a part of the reservoir of latent virus. It is likely that a combination of antilatency mechanisms will be needed, Dr Margolis indicated. High throughput screening has been used to detect compounds with the potential to disrupt latency alone or as a complement to agents used in studies to date. Candidates identified include other HDAC inhibitors as well as other compounds previously investigated for their anticancer properties, such as farnesyl transferase inhibitors and bromo domain inhibitors. According to preliminary data, "it appears we might be able to assemble different strategies to disrupt latency and test them in combination," Dr Margolis said.

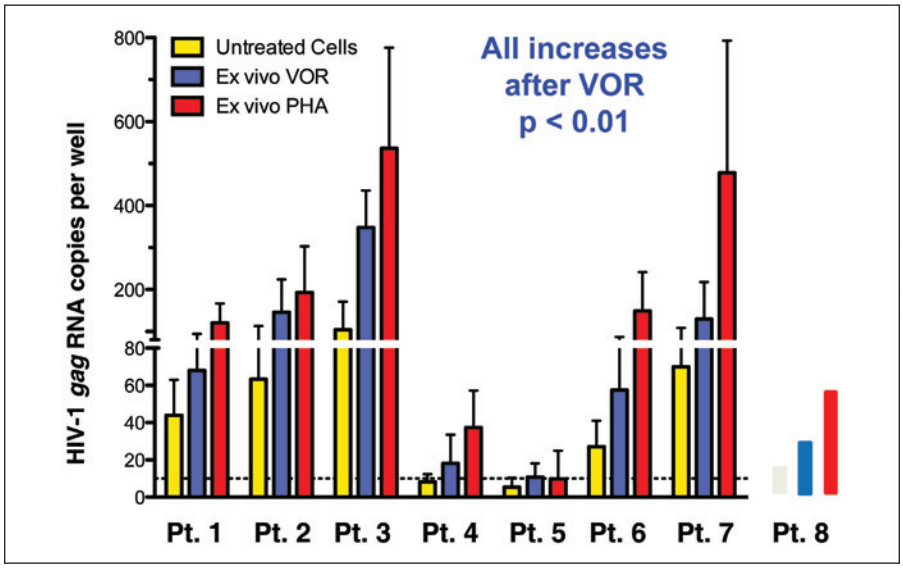


Figure 3) HIV RNA increased with antilatency agent

More Challenges

A further step in testing antilatency agents is the development of appropriate model systems, he remarked. Various cell and animal models are being evaluated.

If an effective antilatency agent can be developed, another necessary step toward viral eradication therapy is to ensure the newly exposed infected cells and virions are cleared from the body. Among options under investigation or being contemplated for boosting the human immune system are agents that reduce its "exhaustion" in responding to HIV and augmentation via vaccine of the HIV-1 specific immune response. "We have tools already to learn how to upregulate the human immune response or even [induce] a synthetic immune response, like an immunotoxin to infected cells, and we have to, step-by-step, learn how these work and how to put them together," Dr Margolis observed. Development of platforms and novel assays will ideally lead to validated agents ready for clinical evaluation.

Epidemiology and Public Health Sciences Plenary

HIV in Zambia and South Africa: Lessons from Community Experiences

Dr. Virginia Bond

Studies conducted in urban communities in Zambia and South Africa highlight how the experiences of people living with HIV are influenced by local attitudes, belief systems, cultures, and health system procedures. In these environments, HIV prevention and treatment are generally considered separate experiences and the promotion of 'treatment as prevention' may not be appropriate, suggested Dr Virginia Bond, Social Anthropologist and Lecturer with the London (UK) School of Tropical Medicine and a Director of the ZambArt Project in Zambia. In fact, she stated, the strategy risks eroding gains made in both domains of health care.

Dr Bond based her observations on information emerging from two studies. The first was a survey designed to "document the HIV landscape" in advance of the HPTN071/PopArt clinical trial, which will assess the effects on infection rates of a universal test-and-treat approach to antiretroviral therapy (ART). Its participants included patients and health care providers. The second study was SEPO II, an evaluation of the health, disability and function of 35 people receiving drug treatment for HIV.

Perceptions of Treatment

In these African communities, the advent of ART is perceived as a positive development that has reduced mortality and has transformed the lives of HIV-positive individuals and their families. Still, there are numerous challenges to treatment uptake in both countries. For patients, awareness that treatment is a lifelong commitment makes the decision to start a difficult one. That side effects were often attributed to missing a dose of medication reflects a strong adherence discourse, particularly in Zambia, Dr Bond noted.

Initiating ART also means committing to regular interactions with strained health care systems. Those encounters are sometimes perceived by patients as less than ideal. Reasons cited included crowded clinics and inadequate attention by busy practitioners, inconvenient appointment times and time-consuming procedures, or rude and judgmental staff. "We have to recognize that treatment as prevention could worsen these encounters with public health care services by increasing numbers," Dr Bond remarked.

Additional and sometimes unique treatment concerns exist in each region. In African cultures dominated by men, women face particular challenges in disclosing HIV-positive status to a partner and accessing ART. Driven by the desire for a cure, PLWH turn to alternative practitioners who often encourage people living with HIV to reject medications in favour of faith healing or immune-boosting herbal remedies. Especially in South Africa, patients carrying ARVs are at risk of being mugged. The stolen drugs may be redirected to the black market where they are sold for recreational use. Those who lose their supply of medication generally cannot have it replaced.

Perceptions of Prevention

In the studies, preventing HIV was widely seen as requiring a combination of strategies, including education and testing. Preventive measures mentioned most often by participants (Table 1) included abstinence, behaviour change, and condom use ("ABC"). Condom use was considered the most practical option, although there are certain cultural barriers to this practice. Medical male circumcision appeared acceptable in Zambia, although there were concerns that young circumcised men feel immune to HIV and take more sexual risks than they otherwise would. In South Africa, medical circumcision is sometimes perceived as "imposed by the West" and a challenge to traditional cultural practices.

Treatment of HIV was rarely cited as a method of preventing viral transmission, except between mother and child. Participants were generally unfamiliar with the acronyms and terms for preventive therapy such as TaSP, UTT, or TcP. (The exception was ABC. One specialist made this suggestion – simply adding "D" for drugs would be appropriate, which reflects how possibly to link treatment and prevention within existing acronyms.) Although they were open to early initiation of ART, Dr Bond stated, a general theme in respondents' comments was that linking treatment and prevention "seems to be at odds with preventive behaviour changes which have been drummed into these populations for so long."

Perceptions of Stigma

Although health gains made through ART can help patients cope with and challenge stigma, visible signs of HIV and AIDS services, such as queues at ART clinics, can actually provoke stigma, Dr Bond recounted. Furthermore, "treatment as prevention appears to have increased the moral tone" around discussions of HIV. "The concept… acts as a catalyst for highlighting the association between having HIV and irresponsible or improper behavior. [It also places] the onus on people with HIV to do the right thing and to contain the transmission of virus, giving others the right to tell people living with HIV how to live. So there is the risk that treatment as prevention could and is creating stigma and redrawing the boundary between 'us' and 'them' that we have worked so hard to pull down," she remarked.

Related Concerns

Overall, Dr. Bond described, HIV treatment and prevention exist in separate "silos" in the Zambia and South African sites studied. However, she observed, the participants frequently expressed the notion that HIV infection and related disease do not exist in isolation. They must be tackled along with contributory social challenges such as substance abuse, transactional sex, youth unemployment, crime, and poverty.

Table 1

Strategies for prevention mentioned by participants

South Africa	Both	Zambia
• Education, sensitization on HIV, treatment and healthy lifestyle • Staying HIV negative • Traditional medicines and immune boosters	• Faithfulness to partner • Condom use • Abstinence • HIV testing/knowing status of self, partner • Treatment of sexually transmitted infections • Prevention of mother to child transmission	• Couple counselling • Control or reduce alcohol intake • Medical male circumcision • Avoid sharing sharp instruments • Faith healing, traditional medicine • Fear of God • Avoidance of 'sexual cleansing' • Masturbation • Taking ARVs

Special Session

Setting Strategic Research Priorities and Processes for the Next Five Years

Jennifer Gunning (CIHR) & Mike Tomlinson (Strachan-Tomlinson)

The Canadian Institutes of Health Research (CIHR), the federal funding agency, is in the process of developing a new strategic plan, Roadmap II.

The CIHR HIV/AIDS Research Initiative, managed by one of CIHR's thirteen Institutes, the Institute of Infection and Immunity, is also in the midst of conducting consultations that will assist in updating their existing strategic plan. Table 1 outlines the existing HIV Research priorities.

Jennifer Gunning, Associate Director of CIHR's HIV/AIDS Initiative, explained that some $23 million is available directly through five funding streams (Table 2). A similar amount is allotted through CIHR overall open competitions and other institutes. At this special session of the CAHR conference, part of a broad national consultation process, participants were encouraged to express opinions on the best research investments for the coming years. They were also asked to recount their positive and negative experiences with CIHR's research programs with a view to improving the direction of research funding in HIV.

Focus groups and an online survey will also allow Canadian HIV researchers and other stakeholders to make suggestions for input to the CIHR HIV multidisciplinary research advisory committee.

With the research agenda is established for the next five years, "we are aiming to have the biggest possible impact on the epidemic in Canada and internationally," Ms Gunning stated.

Table 1
HIV Research Priorities through 2013

Thematic priorities	Target populations
Health systems, services and policy	People living with HIV/AIDS
Resilience, vulnerability and determinants of health	Gay men
Prevention technologies and interventions	Injecting drug users
Drug development, toxicities and resistance	Aboriginal peoples
Pathogenesis	Prison inmates
Issues of coinfection and comorbidity	Youth at risk
	Women at risk
	People from countries where HIV is endemic

Table 2
CIHR HIV/AIDS Funding Streams

Health services & population health research (5.7 M)
Canadian HIV Trials Network (4.5 M)
Community-based research (3.1 M)
Biomedical and clinical research (7.5 M)
Canadian HIV Vaccine Initiative (3.3M)

Red Ribbon Award 2014

Darien Taylor: 25 Years of Advocacy

The 2014 Red Ribbon Award was presented to Darien Taylor, who recently retired after some 25 years as an advocate for treatment, research, patient education, peer support and improvement of the quality of life for those living with HIV/AIDS. Among her many endeavours, Ms. Taylor co-chaired AIDS Action Now, co-founded Voices of Positive Women, worked with provincial and federal health ministries and was the director of program delivery at CATIE.

On presenting the award, Dr. Robert Hogg, CAHR president, said that Ms. Taylor "continues to be a positive voice in the HIV community while advocating for effective treatments… We can think of no one more deserving."

Ms. Taylor remarked that she believed one of the most significant contributions she has made is in ensuring the view of the individual with HIV is represented in research. She said that she "strived to add a bit of counterweight to the inevitable power imbalance inherent in research, by looking around me to create opportunities for people who live with HIV and especially women with HIV to understand, ourselves, more about research and the science… having some say in the direction of that research." She encouraged conference participants to review "some of the innovative work being done by or with people with HIV that is on display."

The Red Ribbon Award has been presented since 2001 for outstanding service to individuals or groups whose research or related work has increased understanding of the treatment and prevention of HIV/AIDS while enhancing patients' quality of life.

CAHR 2014

23rd Annual Canadian Conference on HIV/AIDS Research

Dr. Marina Klein

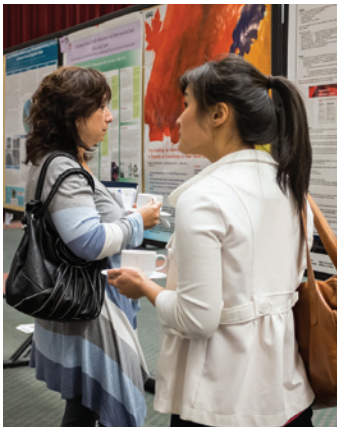
Conference Co-Chairs, Richard Elliott & Mark Wainberg

Dr. Catherine Hankins

Dr. Virginia Bond

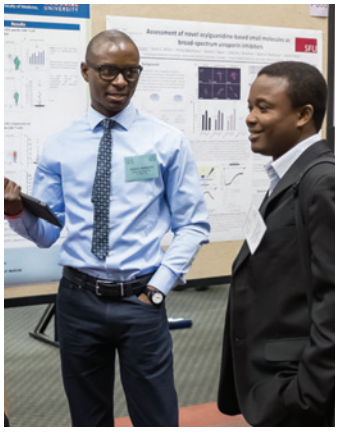
Jennifer Gunning (CIHR) & Mike Tomlinson (Strachan-Tomlinson)

Dr. Richard Parker



Open poster viewing

Dr. David Margolis



Open poster viewing

Continued from page 1

government. "It should have been clear that those ringing declarations of commitment to human rights, to effective responses and bold action, were likely to run into some trouble."

Impediments

Today, he asserted, government actions are actually impeding efforts to fight the epidemic. If the government were, committed to bold, evidence-based action, it would be scaling up access to prevention technologies and education, treatments for HIV and harm reduction measures such as needle and syringe programs and supervised injection services, he indicated.

Several structural factors and public policies in Canada block effective measures to prevent or treat HIV. "If we do not address those structural factors we will simply never harness the benefit of all the technologies we have, no matter how much money we may mobilize to actually deliver testing, treatment and prevention," Mr. Elliott observed. He offered several case studies illustrating the importance of addressing those structural factors and creating what has been called an "enabling environment" for an effective HIV response.

The first of these is the ongoing overextension of the criminal law in relation to HIV non-disclosure. The Supreme Court of Canada stated in 2012 that an HIV-positive person must disclose his or her status to a sexual partner unless both a condom is used during the encounter and his or her viral load is low to undetectable. That both conditions must be fulfilled to avoid prosecution and permanent designation as a sex offender has led to several miscarriages of justice, Mr. Elliott stated. He lauded the May 2, 2014 consensus statement by a group of 70 Canadian scientists that Canadian criminal law goes too far[1], to be released at this year's CAHR conference. The statement agrees with those of other international bodies such as UNAIDS and the Global Commission on HIV and the Law.

Fortunately, a recent case in Nova Scotia highlighted the role and weight of scientific evidence in the legal analysis. In that case, a medical expert testified that there was no "realistic possibility" of HIV transmission to the sexual partner of an individual with an undetectable viral load, despite the absence of a condom. The defendant was acquitted. "We need scientists willing to come forward and, based on the science, take a firm position about what the law should be and not be," Mr. Elliott said. He suggested this would be essential to eventually rectifying the flawed decision of the Supreme Court that unjustifiably has extended the criminal law.

Interestingly, science was critical to the decision of the Supreme Court that blocked the federal government's "arbitrary" attempt to discontinue the exemption of Insite, the supervised injection site in Vancouver, from the prohibition against possession of controlled substances. The court stated that Insite's operation did not undermine, but actually supported, public health and safety. "What was key to securing that victory… was the extensive, authoritative, carefully compiled rigorous evidence about the harms at issue and the great success of this health service in reducing them," Mr. Elliott indicated.

Science is also helping at the global level to undermine the damaging "war on drugs" and the resistance of too many states to harm reduction. At the recent UN Commission on Narcotic Drugs, delegates heard evidence that countries that have implemented harm reduction measures have substantially reduced HIV incidence among people who inject drugs. Despite the evidence, Canadian government representatives at the meeting staunchly resisted references to harm reduction in the consensus resolution. Similarly, while it has been shown that harm reduction measures in Canadian prisons would likely help reduce the shockingly high HIV and hepatitis C prevalence in this population, current federal policy makers have refused to introduce needle and syringe programs. "Just as in the case of Insite, we cannot let criminal prohibitions on drugs and drug use go so far as to deny people access to evidence-based health services," Mr. Elliott asserted.

Elliott concluded by postulating that we may soon enter a new, sixth phase of the HIV response in Canada. There has been a move toward having the Canadian public health response to HIV/AIDS integrated with that of other health issues, thereby "collapsing HIV-directed funding into larger health funding envelopes," Mr. Elliott noted. He indicated that the "integration" agenda cannot become an excuse for fail to recognize the exceptional challenges posed by HIV/AIDS, and further watering down the commitment to basing the response on human rights, which rightly have been at the core of HIV "exceptionalism," transforming the way structures and policymakers respond to a public health challenge.

The Challenge

Among HIV/AIDS activists, there has been a consistent and instructive insistence on human rights and how those norms must transform policy, programs and practice. HIV researchers must work in concert with HIV/AIDS and human rights advocates to present scientific evidence that will appropriately counter current case law and public policies based in ignorance and discrimination, Mr Elliott emphasized. In closing, he encouraged the government "to brace the politics of evidence, of human rights, of courageous leadership against stigma and discrimination, against the politics of criminalization and marginalization of those most at risk and in need of care."

Reference

1. Kuehn BM. Opioid prescriptions soar: increase in legitimate use as well as abuse. JAMA, 2007. 297(3):249-51

CAHR bestows the honour of the Mark Wainberg Lecture to pay tribute to Dr. Wainberg's ongoing contributions, and to recognize the efforts of others in the research community who exemplify the same traits of excellence, perseverance, and commitment to the cause of finding innovative and groundbreaking ways to address the epidemic.

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