JCI The Journal of Clinical Investigation

Myron Cohen ponders path to HIV prevention

Brooke Grindlinger

J Clin Invest. 2009;119(5):1054-1054. https://doi.org/10.1172/JCI39425.

News

In late March, more than 850 HIV/AIDS researchers from around the globe convened in Keystone, Colorado, to mark the 25th anniversary of the Keystone Symposia's first HIV/AIDS conference in 1984. While efforts to develop an HIV vaccine or cure are ongoing, the use of antiretroviral therapy (ART) not only to treat established HIV-1 infection but also as a pre- and postexposure prophylactic measure was dynamically discussed by attendees. The JCI spoke with conference speaker and University of North Carolina at Chapel Hill researcher Myron Cohen (Figure 1) about this emerging new prevention strategy, which is fast gaining ground in the HIV/AIDS research community. JCI: What lies at the heart of this surprising inability to stem HIV transmission? Cohen: Reducing HIV incidence has proven a monumental challenge. Currently, we think that about 4–6 new people get infected for every person we treat. While we have made some progress in HIV prevention, we need better biological tools and a vaccine. JCI: Current guidelines recommend ART for infected individuals with low CD4+ T cell count, high viral burden, and clinical symptoms of advanced disease. Where do you stand in the debate about initiating treatment early versus late during disease progression? Cohen: ART is to be initiated before health is compromised. Observational studies suggest that starting ART early (CD4+ T cell count >350 cells/mm3) […]

Myron Cohen ponders path to HIV prevention

In late March, more than 850 HIV/AIDS researchers from around the globe convened in Keystone, Colorado, to mark the 25th anniversary of the Keystone Symposia's first HIV/AIDS conference in 1984. While efforts to develop an HIV vaccine or cure are ongoing, the use of antiretroviral therapy (ART) not only to treat established HIV-1 infection but also as a pre- and postexposure prophylactic measure was dynamically discussed by attendees. The *JCI* spoke with conference speaker and University of North Carolina at Chapel Hill researcher Myron Cohen (Figure 1) about this emerging new prevention strategy, which is fast gaining ground in the HIV/AIDS research community.

JCI: What lies at the heart of this surprising inability to stem HIV transmission?

Cohen: Reducing HIV incidence has proven a monumental challenge. Currently, we think that about 4–6 new people get infected for every person we treat. While we have made some progress in HIV prevention, we need better biological tools and a vaccine.

JCI: Current guidelines recommend ART for infected individuals with low $CD4^+$ T cell count, high viral burden, and clinical symptoms of advanced disease. Where do you stand in the debate about initiating treatment early versus late during disease progression?

Cohen: ART is to be initiated before health is compromised. Observational studies suggest that starting ART early ($CD4^+$ T cell count >350 cells/mm^3) has benefit, especially in preventing noninfectious cardiovascular complications common in these populations. I am leading a randomized, controlled trial in multiple resource-constrained countries to address when to start ART. We will also determine whether early ART at higher $CD4^+$ T cell count will reduce HIV transmission from a treated patient to their uninfected sexual partner. A total of 1,750 HIV-discordant couples will be followed for 5 years to determine both the feasibility and durability of this intervention. I'll form a final opinion based on the data we collect.

JCI: What has prompted researchers to consider ART as a form of pre-exposure prophylaxis (PreP) in uninfected, high-risk individuals?

Cohen: Trials of PreP with ART are driven by several ideas. First, the drugs are now safe enough to offer to HIV-negative people who might be exposed to HIV, and drug side effects would not be expected to preclude "pleasure." Second, several ART drugs achieve high concentrations for long periods of time in the genital tract, where they should be available to block HIV acquisition. Third, studies with rhesus macaques strongly suggest this approach will work if people reliably take their pills. Ongoing trials employ tenofovir or tenofovir plus emtricitabine because of the safety and anticipated efficacy of these drugs. Another PreP approach involves the use of topical antimicrobial agents, which avoids systemic ART exposure. In addition, slow-release cervical rings impregnated with antiviral agents, which might afford a woman several weeks of protection from HIV with one application, are in development by the International Partnership for Microbicides.

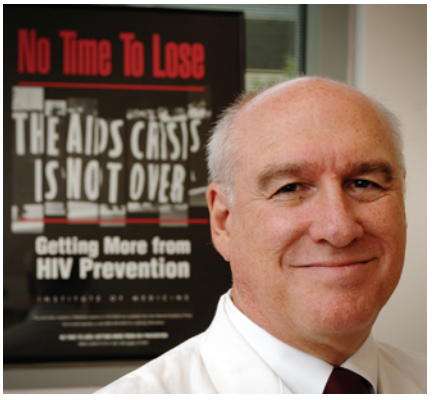

Figure 1
Myron Cohen is leading an NIH-sponsored clinical trial to determine whether antiretroviral therapy can durably prevent HIV transmission to sexual partners. Image credit: Dan Sears, University of North Carolina, Chapel Hill, North Carolina, USA.

JCI: If pre-exposure ART prophylaxis were implemented, what challenges would you anticipate?

Cohen: All too often we develop great biomedical strategies that do not realize the proper benefit for individuals or the public. If PreP works, I expect that the highest-risk groups would be provided some sort of time-limited access to therapy, with counseling and education. However, PreP delivery will require ongoing safety assessment for the individual and real-time, large-scale studies to ensure that communities where PreP is rolled out do not experience an increase in de novo HIV resistance. A concern is that someone who acquires HIV during PreP could develop resistance and transmit the resistant organism to one or more sexual partners. There will be a substantial cost to implement PreP, and it will be hard to justify PreP in communities where ART is not available or rationed for people with HIV or AIDS.

JCI: Some ARTs have been reported to have adverse side effects on bone, liver, and renal function. Would you anticipate opposition to their pre-exposure use?

Cohen: We will need to marry PreP to education to reduce unwanted ART exposure; with reliable and proper use of condoms, PreP will be unnecessary. We will need to determine how few doses of PreP would be required and whether people adhere to intermittent or coitally dependent dosage schedules. These issues, which are not trivial, reinforce the need for development of a topical ART microbicide so that people can have a choice of prevention approaches.

JCI: How do you stay motivated in a field that continues to face so many hurdles?

Cohen: Tenacity. For every possible idea, there are least 10 reasons why the idea won't work. But investigators in the HIV prevention field tend to be indefatigable. Just because we have no HIV vaccine today does not mean we will never have one. The idea of "ART for prevention" or "treatment as prevention" is now at its zenith. Our research group has been working on this idea since azidothymidine was in development in the late 1980s. Seeing the idea tested in clinical trials is both thrilling and rewarding. And as you can tell, I believe we will see a benefit.

Brooke Grindlinger