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GC News is a forum for exchange on new HIV prevention options, especially for women.

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Global

GCM speaks with outgoing Director, Lori Heise

Interview by Deborah Baron

You've been a women's rights advocate long before working in HIV. What was the "aha" moment that got you focused on the need for female-initiated HIV prevention methods?

It was 1991, and I was working on domestic violence issues as they related to international health questions. I was just entering the HIV field, and looking at the role that violence played at compromising women's ability to protect themselves from HIV. At the time, people believed that male condoms were the answer to the AIDS epidemic.

I was doing a workshop at a USAID conference on the implications of women's economic and physical vulnerability on HIV prevention. Most of the conference focused on addressing the challenges of supply chain and getting enough condoms in Africa. There was no space for dialog on the broader issues, and they even slotted my workshop during the open bar reception. I didn't think anyone would come. Instead, the room was packed with peer educators and others working on the frontline. It was the only space where women could discuss issues that reflected their reality on the ground.

One Ugandan peer educator articulated these women's needs so eloquently. She stated simply, "that by asking women to use condoms, you are giving women the choice between not having children and not being exposed to HIV—which was really NO choice at all."

I told her and the other women in the room that I would find out on their behalf what other HIV prevention options are possible. That was the moment I said to myself, "AHA---maybe we need a new tool to help women protect themselves."

What are your top few moments in GCM history?

GCM's greatest moments arise from our ability to anticipate and shape the field by talking about issues early and bringing them to the forefront. Then eight months later, people are talking about an issue and soon we have changed the field. For example, GCM has really grappled with issues around ethics of clinical trials and standards of care for trial participants. We pushed the envelope on community involvement. GCM was one of the first groups to make an evidence-based case around the potential public health benefit of partially effective products. We were able to show that a modestly effective product used consistently could be more effective than a highly efficacious product that is NOT used consistently.

Another big moment was when GCM got its first major grant for $1 million USD from the Ford Foundation in 2002. Up until then, we had been piecing together funding from individual donors. This grant was a huge organizational step for us, and allowed us to hire more staff and expand our programs.

Lastly, I'm really proud of the work we did to get all lubricant manufacturers in the United States to remove nonoxynal-9 (N-9) from sexual lubricants. It was probably the advocacy campaign that had the single greatest public health impact almost immediately.

As the microbicides field has evolved and matured over the past 15 years, what old challenges still remain? What new challenges are emerging?

One old challenge is the disconnect between the people doing cutting edge science and the reality of women's lives. There are still too many assumptions about what women will and will not do, products they will and won't use, and beliefs that women won't use gels in certain societies, such as in places that practice dry sex. Evidence shows us otherwise, but we still need to do more to bridge science and the realities on the ground.

The new challenges emerging are around managing the special challenges of ARV-based products. If the most efficacious products require people to know their HIV status, that is going to present enormous challenges around scaling-up access to counselling and testing.

What are you planning to do next?

I'm planning to take time to finish my PhD in Epidemiology at the London School of Topical Medicine and Hygiene.

Additionally, I want to concentrate with greater depth and focus on some of the research ethics issues that I first worked on at GCM. I'm particularly interested in developing a new framework related to inform and guide research related to public health and HIV prevention.
Historically, research ethics is grounded in medicine and therapeutic drugs for sick people. I want to scope out a middle area that addresses prevention research for healthy people.

What excites you about GCM's incoming Director, Yasmin Halima?

Historically, the field has been quite small, with the same 10-20 people having conversations for the past decade. The notion of having new eyes and adding a new voice to the conversation is very exciting.

Yasmin will add a fresh outlook to the field, bringing with her lots of lateral experience around PrEP and AIDS treatment.

I'm excited that we have a non-American at the helm of GCM. She'll offer new ways to approach the work and the particular challenges of the field.

Our next issue will feature an interview with Yasmin Halima, GCM's incoming Director!

Research Update

Tobacco, "Plantibodies" and New Microbicides?

Could microbicidal agents be grown in tobacco plants? Research in both North America and Europe shows that this concept is not only viable but also potentially highly cost effective. In 2006, researchers at University of London[1] showed that Cyanovirin-N (CV-N) can be produced in significant quantities in transgenic tobacco plants. CV-N can bind to HIV's protein envelope at the gp120 site, the "hook" it uses to attach to the human cell. By blocking that hook, CV-N effectively prevents HIV from being able to latch onto a human cell and, thus, could prevent infection. Pre-clinical trials in macaques have shown that CV-N, applied either rectally or vaginally, can provide some protection from sexually transmitted simian HIV (SHIV), a "monkey version" of HIV. The latest research published in May, 2009 suggests that combining CV-N with an antibody called b-12 may make the combination more potently protective than either component alone.[2]

An article published in PNAS April, 2009[3] detailed NIH funded research on griffithsin (GRFT), another HIV entry inhibitor microbicide candidate grown in tobacco plants. GRFT is in the class of proteins known as neutralizing monoclonal antibodies. GRFT has been shown in pre-clinical trials in macaques to protect animals against vaginal infection with SHIV.

Researchers have been exploring monoclonal antibodies for HIV prevention for the last decade but the compounds were simply too costly to put into clinical trials. Now efforts to generate production by means of transgenic plants are showing success. Some refer to these compounds as "plantibodies".

Transgenic plants are genetically modified to contain one or more genes from a different species. Gardeners and crop breeders achieve a version of this process when they create hybrids of two plant species. In the laboratory, the process is done with recombinant DNA technology -- that is, by combining DNA sequences that do not normally occur together. Inserting these "designer DNA" combinations, scientists can create plants with improved nutritional quality, insect resistance, or disease resistance. Golden rice, for example, was designed to correct dietary vitamin A deficiencies.

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[1] Sexton A, Shattock R and K Ma. Transgenic plant production of Cyanovirin-N, an HIV microbicide, poster presented at St George's, University of London Research Day, 7 December, 2006, available online at http://www.researchday.sgul.ac.uk/prizewinners/A.Sexton%20et%20al%20poster.pdf

[2] Sexton A, Harman S, Shattock RJ and J Ma. Design, expression, and characterization of a multivalent, combination HIV microbicide. FASEB Journal. .2009; 0: fj.09-131995v1, available on line at http://www.fasebj.org/cgi/rapidpdf/fj.09-131995v1

[3] O'Keefe B, Voidani F, Buffa V et al. Scaleable manufacture of HIV-1 entry inhibitor griffithsin and validation of its safety and efficacy as a topical microbicide component. Proceedings of the National Academy of Sciences of the United States. April 14, 2009 vol. 106 no. 15 6099-6104, available on line at http://www.pnas.org/content/106/15/6099.full

Corn, tomato, rice, potato and tobacco plants have all been genetically engineered in the last twenty years to produce antibodies, blood products, and human and veterinary vaccines that are now on the market. Plant-derived pharmaceutical proteins for treatment of rabies and Hepatitis B are also close to commercialization.

In the most recent study, O'Keefe et al. showed that one gram of GRFT was produced for each kilogram of transgenic tobacco leaf grown. At that rate, it is conceivable that large-scale agricultural production of transgenic tobacco plants might affordably produce enough of these potential microbicides to satisfy the demand of those most in need of them at a price that does not exceed the cost of a male condom.

GCM in Action

"HIV Prevention Research Ambassadors" training in Kisumu, Kenya

The Global Campaign for Microbicides (GCM), in collaboration with Kenya Medical Research Institute (KEMRI) and staff from FEM-PrEP[4] Bondo trial site, brought 24 participants to together on May 12-13 for a two-day skills building workshop in the Nyanza province of western Kenya. One participant described the lively mix of presentations, question and answer sessions, and small group discussions as an "eye opener for me on HIV prevention research." Others said they were inspired with new ideas about how they could engage with other stakeholders in the research processes.

Facilitators started with a discussion of the potential impact that microbicides and PrEP, as new HIV prevention tools, could have in Nyanza Province, which has the highest HIV rates in Kenya. They also highlighted the feminization of the epidemic and the need for a woman-initiated response. To enhance participants' understanding of prevention research, the facilitators took them though the clinical trial process, explaining what each phase seeks to establish and the average trial size for each phase. Day Two revolved around issues of community involvement and advocacy. Clinical trial staff from KEMRI and FEM-PrEP's Bondo trial site shared case studies of their sites' community involvement work. This led to discussion of the range of ways in which advocates could engage with researchers as "HIV prevention research ambassadors" who bring their communities' perspectives to the table.

Noted the such communication would have to be reciprocal, participants agreed that they needed regular updates from the trial sites on HIV prevention research developments in their province and community to fulfill this role successfully. They also noted areas of serious concern that had been expressed in their communities already including:

- desire for greater male involvement in the clinical trial processes as well as in promotion of new prevention tools, when they become available.

- concern about the potential effects of long-term ARV- based prevention (PrEP) and microbicides) use by HIV negative people -- such as potential toxicity, impact on future fertility, stigmatization and the possible development of drug-resistant virus if users unknowingly continue PrEP use after becoming HIV positive

- issues around compensation for trial participants – Is it enough? Too much? Does it give participants an incentive to enroll in more than one trial at a time, which can generate health risks and inaccurate research findings?

Many participants voiced the need for further training, especially as this was the first workshop they attended on HIV prevention research. "I hope that this is not the first and last training, said one participant. "I have benefited a lot from this workshop. It has cleared my foggy areas in scientific research…"

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[4] More information on the FEM-PrEP trial is available at http://www.prepwatch.org/pdf/Trials/FEMPrEP_Issue%201_Jan2009.pdf

Materials Update

New GCM Materials on PrEP

GCM is developing a range of new materials as part of our decision to address the full range of new HIV prevention technologies (NPT) in the context of women's prevention needs. We are happy to announce that the first of these are ready for use. Please go you our website to see:

PrEP: What is it? How may it help women? a new GCM powerpoint presentation complete with slides and easy-to-read script available at http://www.global-campaign.org/clientfiles/GCM_IntroToPrEP.ppt

As with all of GCM's standardized powerpoints, this is designed for use by advocates who do not have a scientific background. We provide these to make it as easy as possible for our civil society allies to provide accurate, accessible information in their own communities.

PrEP: What Does It Mean For Women?: a new, two-page (one sheet) GCM fact sheet, also designed for use by advocates and other civil society groups available on-line at http://www.global-campaign.org/clientfiles/FS-PrEP[E].pdf

As with all GCM materials, reproduction of these tools is encouraged. Please feel free to download them, translate them, adapt them for local audiences and use them in any way that will make this information more widely available. They are provided as a free resource to the field. Feedback on these is also welcome and can be sent to info@global-campaign.org

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What is GCM Doing this Month?

Microbicides Research Literacy Training: Nairobi, Kenya; Lusaka, Zambia; Mazabuka, Zambia

18-27 June, Kenya & Zambia

GCM staff members will travel to Nairobi, Lusaka, and Mazabuka to conduct Microbicides Research Literacy training for civil society advocates and clinical trial staff. This training will enable participants to better communicate complex research concepts to trial participants, communities, and other stakeholders. These communication skills are vital for ensuring that trials can move forward successfully, so that new prevention options can be found.

Uganda Female Condom Advocacy Workshop

23-25 June, Kampala, Uganda

The Center for Health and Gender Equity (CHANGE) and GCM are jointly convening a Female Condom Advocacy Workshop that will be attended by over 30 Ugandan NGOs on 23-25 June. The three-day session is designed to increase coordination and build advocacy skills among civil society organizations that support female condoms, and pave the way for a coordinated advocacy campaign to strengthen government and donor support for female condom programming. The workshop will open with welcoming remarks by Mubarak Mabuya, of Uganda's Ministry of Gender, Labor, Social Development. Vastha Kibirige, coordinator of the condom unit for the Ministry of Health's STD/AIDS control program, has also

been invited to discuss Uganda's new female condom initiative. It will also include visits by participant delegations to three major donor entities.