



ALLIANCE FOR MICROBICIDE DEVELOPMENT

16 March 2007, Volume 8, Number 10

The Alliance for Microbicide Development *News Digest* is an **unedited** compilation of:

- Media coverage of microbicides;
- Abstracts of articles on microbicides and relevant science in peer-reviewed journals;
- Material on other reproductive health and HIV prevention technologies, including HIV vaccines; and
- Matters of policy and politics with importance for microbicide research, development, and advocacy.

Its purpose is to:

- Raise awareness around the range of opinions and information about microbicides disseminated in the press and scientific journals; and
- Provide a neutral, objective basis for decision-making and evidence-based advocacy.

The *News Digest* is produced in a web-based format. Readers can view individual articles or complete issues at <http://www.microbicide.org/publications/> and may also search by keyword for articles included in issues of the *Digest* created after 27 January 2006, at <http://www.microbicide.org/publications/search.html>. Should you wish to be removed from the *Digest* distribution list, please advise us at digest@microbicide.org. We welcome comments, questions, and ideas about other microbicide-relevant topics we might cover, services we might provide, and better ways of providing them!

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1. ALLIANCE UPDATES AND COMMUNITY NEWS

Continuing coverage of the closure of the Phase 3 cellulose sulfate trials

EDITORS' NOTE: *Because there has been a great deal of coverage of the closure of the cellulose sulfate trials, the Alliance has opted to be selective about including ongoing coverage in the Digest. However, we believe that the following two articles merit particular attention:*

"Recent public statements from the IAS: Microbicide trials halted"

Date: March 2007

Source: *IAS Newsletter*

The IAS acknowledges the February 2007 announcement that two Phase III trials of Ushercell (a cellulose sulfate based topical gel being testing for HIV prevention in women) have been halted due to preliminary results at some sites indicating potential increased risk for HIV among women who use the compound. The findings of increased risk were identified at some sites in a trial sponsored by CONRAD, a cooperating agency of USAID administered through the Department of Obstetrics and Gynecology at Eastern Virginia Medical School in the United States. The CONRAD trial was being conducted in South Africa, Benin, Uganda and India. While emphasizing the urgent need for the timely

development of an effective **microbicide** to protect women from HIV infection, the IAS also recognizes the utmost importance of safety, and applauds the decision to halt the studies to evaluate the preliminary findings.

Family Health International, sponsor of the second halted trial in Nigeria, had not found similar results but halted the trial as a precautionary measure, given the preliminary results in the CONRAD trial. At this point, it is not clear why the use of cellulose sulfate was associated with increased risk for HIV infection among women in the CONRAD-sponsored trial. Earlier trials of the same compound involving 500 participants did not indicate safety concerns.

"While extremely disappointing, this setback is also an opportunity to learn why some women who used Ushercell were found to be at increased risk of HIV infection," said Dr. Pedro Cahn, President of the IAS and Director of Fundacion Huesped in Buenos Aires, Argentina. "This will strengthen future **microbicide** research and increase our overall knowledge of how such compounds work."

"The importance of developing a safe and effective **microbicide** to protect women from HIV infection cannot be understated," said Dr. Cahn. "We must give women the tools to protect themselves, independent of their partners' actions."

The halted trials were two of six Phase III **microbicide** trials underway at the start of 2007. Four additional Phase III trials of other candidates are ongoing.

Further data on **microbicides** and other biomedical prevention tools will be discussed during the upcoming 4th IAS Conference on HIV Pathogenesis, Treatment and Prevention in Sydney.

"A microbicide conundrum"

Author(s): David Gilden

Date: March 2007

Source: *Community HIV/AIDS Mobilization Project HHS Watch*

<http://www.champnetwork.org/index.php?name=news>

The January 31 announcement came like a bolt out of the blue: Researchers had prematurely terminated the two large efficacy trials for the **microbicide** cellulose sulfate. The trials were expected to show that vaginal applications of the **microbicide**, commercially known as Ushercell, would reduce HIV transmission during sex. But in one trial, women using cellulose sulfate paradoxically had higher rates of HIV acquisition than those using an inactive placebo gel. The Gates Foundation and USAID had poured \$24 million into the trial program. Jeff Spieler, Chief of USAID's Research, Technology and Utilization Division, Office of Population and Reproductive Health, reacted to the closure by saying, "I am surprised and disappointed by these findings given the pre-clinical effectiveness and safety profile of CS [cellulose sulfate] and its safety profile demonstrated in Phase I trials."

Cellulose sulfate, a derivative of cotton, is a member of the group of promising **microbicides** technically known as "anionic polymers." These compounds attach themselves to viral surfaces and disrupt virus-cell binding. They are active against HIV and other STDs, including such bacterial infections as gonorrhea and Chlamydia as well as herpes simplex virus. Some of the candidate **microbicides**, including cellulose sulfate, have contraceptive potential. They disrupt sperm membrane function, causing reduced mobility and egg penetration. Two other anionic polymers,

Carraguard and PRO 2000, are also the subjects of advanced **microbicide** trials.

The closed trials tested cellulose sulfate under particularly rigorous conditions. One trial, sponsored by CONRAD (associated with the Eastern Virginia Medical School) was recruiting 2,574 HIV-negative women in India, Benin, Uganda and South Africa. The women had to have had at least three male sex partners in the three months before enrollment and to have averaged at least three sex acts a week. Most, but not all, were commercial sex workers. Half of the trial participants applied a cellulose sulfate gel prior to having sex. The remaining participants used a placebo gel without the cellulose sulfate. Neither group knew which gel they had been given. All participants also received regular safe-sex counseling and supplies of condoms. The other trial was sponsored by Family Health International (FHI) and took place in Nigeria. This 2,160-person trial followed a similar design except that enrollees needed to have had two or more male sex partners in the previous three months.

The CONRAD trial was the one that observed a higher rate of new HIV infections among the cellulose sulfate recipients. It is important to note that CONRAD recorded only 35 HIV transmissions in all. Both trials together were only half-enrolled when they closed. Data collection is not complete and CONRAD foresees no further release of information on its trial until next fall at the earliest. The two trials suffered from serious statistical weaknesses: HIV rates during the trials were lower than anticipated and pregnancy rates higher. The low rates of HIV transmission made it difficult to detect any effect of the **microbicide** unless the trials enrolled more women or followed them longer. Since pregnancy led to temporary exclusion from the trials, the resulting reductions in gel use further undercut the trials' statistical power.

In light of the small number of HIV cases to work with, Lut Van Damme, the lead researcher for the CONRAD trial commented, "The recommendation to close was a big shock. We chose to err on the side of women. When we have the final data, it may show that cellulose sulfate was not unsafe. But even if it kept going, the trial may not have been large enough to show efficacy."

HIV, Pregnancy and Trial Design

The cellulose sulfate trials were designed with the expectation that HIV transmission rates among placebo recipients would be at least four percent per year of observation. The rate instead was around 2%. At that low incidence, the trials would have had to expand enrollment several fold to demonstrate that cellulose sulfate was effective. Already, FHI had stopped enrollment at its Nigerian sites and was preparing new sites in South Africa. CONRAD had contingency plans to shift enrollment to southern Africa and increase total trial size.

It has proven very difficult to anticipate the background HIV incidence rate in the populations enrolling in prevention trials. Ten years ago, large trials for nonoxynol-9 vaginal **microbicides** were conducted in similar populations as the present cellulose sulfate trials. The trial designs were also comparable: participants received similar safe-sex counseling, condom provision and STD treatment. Yet, the observed HIV transmission rates in the nonoxynol-9 trials were much higher: 7% to 10% - and up to 14% among one trial's nonoxynol-9 recipients. (Nonoxynol-9 was the original big **microbicide** failure-see below.)

High community HIV levels do not mean that there are high current rates of transmission. An HIV epidemic reaches a mature stage when most people with behavioral and biologic risks for HIV are already infected.

It has proved very challenging to identify the best populations for testing **microbicides**. In the words of Lori Heise, director of the Global Campaign for **Microbicides**, "High HIV incidence occurs in newly exposed populations, where

the epidemic is on the cusp. Vaccines and PrEP [pre-exposure prophylaxis] trials can recruit across settings. They can recruit men, including those who have sex with other men, and IV drug users. The current **microbicide** trials recruit only among women who are at risk for HIV through vaginal sex. They need women who are at high risk but consistently unable to use condoms. This is a very narrow group - even sex workers can use condoms well."

Pregnancy has proved another stumbling block. The FHI trial noted a pregnancy rate of 30% per year of observation. It also found that the women in its trial said they used their gel, whether placebo or active, for 80% of all sex acts. Reported condom use increased from 60% to 90% during the trial. A previous trial with monogamous couples in California found that cellulose sulfate compared favorably as a contraceptive with nonoxynol-9, the only vaginal agent marketed in the US. With very frequent sex, though, high pregnancy rates over fairly short periods could occur even with an average 80% usage, especially if there was a tendency to dispense with both condoms and gel on the same occasion.

Pregnant women were excluded from receiving their assigned trial product because reproductive toxicity studies have yet to be conducted on cellulose sulfate. This lapse meant that women did not have the **microbicide** when they appear to be particularly vulnerable to HIV. Despite their suspension, the trial counted them as if they were still part of their assigned trial cohort because of the researchers' planned "intent-to-treat" trial evaluation. "Intent-to-treat" is usually a valuable way to analyze medical products. It takes into account the fact that, in the real world, many people stop using products due to side effects or inconvenience. This trial, though, involved involuntary discontinuations that would not have occurred in the real world. Including the pregnant women in the trial results further weakened the trials' ability to show a benefit from cellulose sulfate.

The Necessary Preliminaries to Advanced Human Trials

The large nonoxynol-9 trials suffered from neither of these issues. There, the problem was that heavy use of nonoxynol-9 increased the risk of acquiring HIV because it irritated the vaginal lining when applied. That increased risk was only apparent in trial participants who on average used nonoxynol-9 more than 3.5 times per day.

The nonoxynol-9 results led to a shake-up in the way **microbicides** are developed. Laboratory reports indicating nonoxynol-9's irritating effects became available only after the human trials had commenced. Since then, candidate **microbicides** have been carefully tested in the lab and in small human studies for signs that they disrupt vaginal surfaces.

Nonoxynol-9 is a surfactant that dissolves viral and cell membranes. Although cellulose sulfate has no such effect, it is a potent inhibitor of blood clotting. Previous cellulose sulfate trials did not notice any signs of vaginal irritation or non-menstrual bleeding. All but two of these trials were small and short, lasting at most four weeks. The major exception is the six-month, 200-person contraception trial conducted in monogamous California couples.

The latest trials took place in a considerably different environment. They involved high **microbicide** use and longer periods of time. Trial enrollees also were much more likely to have untreated STDs. Under such conditions, vaginal irritation and lesions would be greatly elevated. Bleeding during sex then would be more frequent. The presence of cellulose sulfate could increase the risk of HIV if it prolonged such bleeding. But this scenario is completely speculative due to the lack of intermediate trials in similar populations. Such "phase II" trials are common in drug development. They confirm the agent's safety within a larger population and provide initial measures of effectiveness.

Van Damme commented, "We moved forward because the previous trials did not indicate safety issues. Only the larger trials can measure HIV transmission endpoint."

Researchers have generally felt that **microbicide** toxicity issues can be resolved with small, quick trials. In contrast, effectiveness is very difficult to measure. There is no preliminary indication of protection equivalent to the viral load declines seen with new anti-HIV drugs. Efficacy for **microbicides** is only observable by comparing how condoms plus **microbicides** decrease HIV rates compared to condoms plus placebo. Considering the effectiveness of condoms alone, that takes a very large trial indeed, even when a suitable high-risk population is selected. Still, cellulose sulfate results show the chances taken when so quickly ramping up.

Some version of phase II trials may be in the offing. According to Heise, "To manage the uncertainty, the field is moving toward a phase II run-in and then rollover to phase III." Such a strategy would imply looking at intermediate results in a moderate-size population before involving thousands of trial enrollees in a full-scale efficacy evaluation.

*A report on the CONRAD trial was presented Tuesday, February 27, 2007 at the 14th Conference on Retroviruses and Opportunistic Infections (CROI): Oral Abstract 106LB: Update on the CONRAD Cellulose Sulfate Trial, Gustavo Doncel and Lut van Damme, CONRAD, Arlington, VA, US. For a video of this presentation, go to the following web page and select the Tuesday session on Late Breaking Trials of New ARVs and **Microbicides***
http://www.retroconference.org/2007/data/files/webpage_for_CROI.htm.

See also the World Health Organization's January 31, 2007 statement about the cellulose sulfate trial closure:
<http://www.who.int/mediacentre/news/statements/2007/s01/en/index.html>.

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2. MEDIA COVERAGE OF MICROBICIDES

"At large: Condoms and choices"

Date: 13 March 2007

Source: *Philippine Daily Inquirer*

Author(s): Rina Jimenez-David

http://services.inquirer.net/print/print.php?article_id=54404

HIV/AIDS has already been recognized as a woman's issue. More women than men are getting infected with HIV, and this is mainly because women, due to biology as well as culture and social status that influence their sexual behavior and decision-making power, are more vulnerable to sexually-transmitted infections.

But why is it that, despite more than 20 years' research into and development of prevention strategies against HIV/AIDS, the number of new infections among women -- and deaths, as well -- continues to rise? An article in the December 2006 issue of *International Family Planning Perspectives* argues that part of the reason may be that strategies have not been attuned enough to the realities of women's lives and situation, and that, ironically enough, too much emphasis has been placed on the use of the male condom as the "most effective" means of protecting oneself from HIV/AIDS infection.

Erica Gollub, a professor of epidemiology, asserts that "successful HIV prevention work among women means the adoption of a woman-centered paradigm, one that is grounded in women's realities and acknowledges gender roles and gender-based power differentials as critical factors in women's ability to make and effect decisions regarding their health and welfare."

Years of research have also shown that "most women around the world cannot control male condom use," says Gollub, "and we have begun to understand that women's attitudes toward and use of protective methods are based on personal, relational, sociocultural and structural factors, with a different mix for each woman."

Indeed, because condoms need to be put on by men -- and it would be difficult to get a man to use a condom without his knowledge or consent -- Gollub notes that "we have now recognized the limits of a sole dependence on the male condom." She says: "Male control over the male condom undermines its real-world impact."

Despite decades of work touting the advantages of the condom -- and it is a very effective means of preventing sexually transmitted infections -- "large-scale male condom campaigns have been inadequate as a public health strategy." Gollub notes that "recent studies of US women at high HIV risk show that the proportion of protected sex acts rarely exceeds 15 percent, a statistic that has not changed over the past decade. Women in developing countries are often not protected at all."

She adds: "Our stubborn insistence on presenting the male condom as a '100 percent method' has played right into the hands of those who argue that advocating male condom use to prevent HIV infection under-serves women because it exposes them to (occasional) failures and does not make the most of women's 'power' in saying no to sex."

"We have seen the credibility of the male condom damaged over the past several years by disinformation campaigns, and the language of reproductive rights twisted to disempower women," recounts Gollub. "Precious resources that could have been used for prevention are now being wasted in countering these attacks. Future HIV prevention efforts should focus on the potential for a given method program or policy to increase a woman's ability to control her reproductive health, rather than on product efficacy values that apply to a narrow set of users under highly manipulated conditions."

There are other, women-controlled "technologies" that offer protection against HIV, including the female condom which is considered to be as effective as the male condom. And while spermicides, which had been looked upon as a promising alternative but have proven to be useless against HIV transmission, Gollub says cervical barriers "hold great promise as risk-reduction tools," mainly because the cervix is more susceptible to HIV infection than the vagina. There is an ongoing large trial to test the effectiveness of a "one-size-fits-many diaphragm." Clinical trials of **microbicides** are likewise underway.

"Widening our approach to include more than the exclusive promotion of the male condom," says Gollub, "means grasping the essential notion that no prevention method will ever be ideal for all women or in all situations."

She asserts: "We are still wrestling with the outdated question of 'which is better?' rather than the considerably more constructive and expedient framework of 'more is better.'"

Gollub says a more efficient next step would be to adopt a "sexual risk reduction" philosophy, "similar to that of the harm-reduction approach to needle-related HIV risk among injection drug users."

Such an approach, she suggests, involves giving women choices when it comes to prevention methods - behavioral (such as reducing the number of partners), product-based (such as alternatives to the male condom) or both - to maximize prevention potential.

"Something is better than nothing," Gollub declares.

While other methods and approaches may not be as effective as the condom against HIV, they "could nevertheless have great individual or public health value if they were used consistently."

In New York, for instance, the State AIDS Institute has "advocated a hierarchical counseling approach that presents available methods that have the potential to reduce STIs and HIV infection, ordered by their efficacy." Such a hierarchy, suggests Gollub, "might place female and male condoms at the top rung, diaphragms and cervical caps on the second rung, and coitus interruptus on the third rung."

Will giving women choices and acknowledging their power to make those choices finally give them the protection they need against HIV infection? What will it take to put HIV prevention in the hands of women -- and not just on the penises of their partners?

"Frederick-based Imquest Pharmaceuticals Inc. gets \$700K grant for HIV study"

Date: 13 March 2007

Source: *The Daily Record (Baltimore, MD)*

Author(s): Karen Buckelew

ImQuest Pharmaceuticals Inc. is using a new grant worth up to \$700,000 to advance its novel HIV preventive closer to human testing among high-risk women in the developing world, where it is needed most. The Frederick-based company hopes its portfolio of three potential HIV **microbicides** will prove effective in preventing HIV transmission from a man to a woman during sex, particularly in areas with high rates of HIV such as Africa. The grant from the **International Partnership for Microbicides**, a Silver Spring-based nonprofit, will fund preclinical testing of the three compounds ImQuest has licensed from a Korean company, said President and Chief Scientific Officer Robert W. Buckheit Jr.

In the developing world, condoms often carry a stigma and women do not always have a voice in whether or not sex is safe, Buckheit said. ImQuest and the partnership are attempting to develop a vaginal **microbicide** in gel or ring form for a woman to apply privately daily or monthly without having to consult with her sexual partner.

Microbicides, said Buckheit, are becoming increasingly popular in the quest to fight HIV and AIDS. Of the 4.3 million new HIV infections worldwide last year, 2.8 million, or 65 percent, occurred in sub-Saharan Africa, according to the World Health Organization.

ImQuest also is hoping to act as lead investigator in a \$10 million collaborative research project that includes a consortium of academic institutions such as the Johns Hopkins University, Duke University and the University of Utah. The consortium is preparing a grant application for submission to the National Institutes of Health to examine issues such as how to stabilize a **microbicide** gel to keep it effective in the body for 24 hours, Buckheit said.

Worldwide, 14 **microbicide** candidates were undergoing human testing as of August 2006, and more than 30 candidates were in preclinical stages, according to the **Alliance for Microbicide Development**, a Silver Spring-based coalition. "The world is still looking for something that will actually work," Buckheit said.

ImQuest's preclinical studies include discerning if the three compounds work best together or if one stands out as particularly effective. If preclinical testing goes well, the company could apply to federal regulators for permission to test the compounds in humans by the end of 2007 or early 2008.

ImQuest's three **microbicide** product candidates are among 68 compounds licensed from Samjin Pharmaceutical Co. Ltd. of Korea in February 2006. The compounds, known as pyrimidinediones, attack HIV in two ways, said Joseph Romano, executive director of research and development for the **International Partnership for Microbicides**. If the virus develops resistance to one of those mechanisms of action, the other will be there to back up the attack, according to Romano. The dual action "creates an increase in potency and effectiveness," he said.

The program is not exactly a cash cow for ImQuest, a 12-employee company that also encompasses ImQuest BioSciences Inc., a contract research organization that provides research services to other companies. Large pharmaceutical companies don't typically work in the anti-HIV **microbicide** field, as the profit margin for such a product where it is needed, in developing countries, is "very small," Romano said. That is where the **International Partnership for Microbicides**, funded by the U.S. Agency for International Development and the Bill and Melinda Gates Foundation, among other sources, steps in.

Buckheit described ImQuest's efforts as a "humanitarian" application for its technology. The company hopes Romano's organization will take over the development of the compounds at some point in their clinical development. "We don't believe these things are money-makers," Buckheit said. "We just don't want them to be money-losers. "

"Indian institute chosen for trials of microbicides"

Date: 13 March 2007

Source: *The Indian Express*

Author(s): Anuradha Mascarenhas

<http://www.indianexpress.com/story/25562.html>

Research on **microbicides** is set to receive a fillip as the US-based National Institutes of Health (NIH) has selected National AIDS Research Institute (NARI) as an HIV/AIDS Clinical Trial Unit (CTU) in India.

Microbicides are compounds developed for women to reduce the transmission of the HIV virus during intercourse. Research on these had suffered a setback with the cancellation of clinical trials in January. In the developing countries, the HIV virus often spreads through unprotected intercourse and educational efforts promoting abstinence, monogamy and condoms have not been very effective.

NARI and eleven other CTUs will now be engaged in research across 17 locations in seven countries to determine whether tropical **microbicides** can help prevent transmission of the HIV virus. "It is a great honour and recognition of the work done by NARI," said R S Paranjape, director of the institute. NARI will now be the official unit for conducting trials on the safety and acceptability of vaginal **microbicides**.

Nearly half of the 39.5 million people living with HIV/AIDS are women. In Africa, women account for 59 per cent of all infected adults. In India, 5.2 million people are infected with the HIV virus and nearly 45 per cent are women, said S M Mehendale, deputy director senior grade, NARI.

NARI is one of twelve institutes named by the National Institute of Allergy and Infectious Diseases (NIAID) as clinical trial units for the **Microbicide** Trials Network (MTN). MTN's clinical research sites are located in Pune, Llongwe, Malawi (two sites), Durban, South Africa (four sites), Cape Town, South Africa, Kampala, Uganda, Harare, Zimbabwe (two sites) and Lusaka, Zambia as well as in New York, Cleveland, Pittsburgh, Philadelphia and Birmingham, Alabama.

"South Africa: Draft plan on HIV and AIDS to be presented this week"

Date: 11 March 2007

Source: *BuaNews (Tshwane)*

Author(s): Nozipho Dlamini

<http://allafrica.com/stories/200703110125.html>

The Health Department will hold a national consultative conference this week to present the final draft of the National Strategic Plan for HIV and AIDS and STIs for 2007 to 2011. Addressing the media in Johannesburg on Friday, Acting Health Minister Jeff Radebe said the conference would ensure that all stakeholders had an opportunity to make an input into the final plan. Minister Radebe made the announcement following the meeting of the National Health Council where a draft plan was presented to the council by Task Team responsible for developing the plan. "We have gone through this extensive consultation process to ensure that as a nation we take ownership of the final document that gets adopted by the new South African National AIDS Council," said Mr Radebe.

The conference will be addressed by the Deputy President Phumzile Mlambo-Ngcuka and is expected to bring together more than 500 representatives from various stakeholders in the HIV and AIDS sector. The primary goal of the plan is to reduce the rate of new HIV infections and mitigates the impact of AIDS on individuals, families and communities.

The plan has four key priority areas which are:

- Prevention;
- Treatment, Care and Support;
- Monitoring, Evaluation and Research and
- Human and Legal Rights

Regarding prevention, Mr Radebe said the aim was to achieve 50 percent reduction of rate of new infections by 2011. "To achieve this, we need to intensify the implementation of prevention interventions aimed at changing behaviour and reduce sexual transmission," he emphasised.

The department, Minister Radebe said, had already made significant progress in expanding services for prevention of mother to child transmission of HIV. To date, 80 percent of primary health care facilities (3382 out of 3663) are

providing the services and government's target is to reach 100 percent by the end of 2007. "We intend to provide an appropriate package of treatment, care and support services to at least 80 percent of people living with HIV and their families by 2011.

The treatment package will include:

- Counselling and testing services as an entry point;
- Healthy lifestyle interventions including nutritional support;
- Treatment of opportunistic infections and
- Antiretroviral therapy

Furthermore, the plan will include a framework for monitoring and evaluation which should measure the collective progress in the implementation of the plan. In the area of research, it will support ethical scientific research into additional tools for the response to HIV and AIDS including vaccines, **microbicides** and traditional medicines.

The minister explained that the council believed that the draft strategic plan provided a sound basis for a discussion among stakeholders at the conference.

"Other microbicides quietly pine away"

Date: 28 February 2007

Source: *Community HIV/AIDS Mobilization Project HHS Watch*

<http://www.champnetwork.org/index.php?name=news>

More trials mean greater development costs for successful **microbicides**, and financing is already tenuous for the loose network of nonprofit organizations, small businesses and academic investigators who conduct **microbicide** research. Just how tenuous was illustrated last fall, when development of a new promising **microbicide**, cellulose acetate phthalate, or CAP, ground to a halt. CAP has a structure related to the sulfated anionic polymers but offers several potential advantages. It is particularly effective at deactivating HIV and does not retard blood-clotting. CAP is widely used to coat pills and considered innocuous.

Scientists at the New York Blood Center spent nearly 10 years and \$10 million doing lab studies. A consortium of research centers led by the Blood Center recently received \$6 million from the NIH to conduct early human trials. But the chief researcher, Robert Neurath, has retired after a dispute with the Blood Center management over research funding. Neurath's retirement left the new human trial consortium in limbo. He now says, "As far as I know, not much is happening now regarding a commercially and medically viable CAP formulation since my efforts have been blocked."

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3. PUBLISHED RESEARCH: MICROBICIDE-SPECIFIC

"Broad-spectrum anti-human immunodeficiency virus (HIV) potential of a peptide HIV type 1 entry inhibitor"

Author(s): Cocklin S, Gopi H, Querido B, et al

Reference: N/A 81(7):3645-8.

Published Abstract: The AIDS epidemic continues to spread at an alarming rate worldwide, especially in developing countries. One approach to solving this problem is the generation of anti-human immunodeficiency virus (HIV) compounds with inhibition spectra broad enough to include globally prevailing forms of the virus. We have examined the HIV type 1 (HIV-1) envelope specificity of a recently identified entry inhibitor candidate, HNG-105, using surface plasmon resonance spectroscopy and pseudovirus inhibition assays. The combined results suggest that the HNG-105 molecule may be effective across the HIV-1 subtypes, and they highlight its potential as a lead for developing therapeutic and **microbicidal** agents to help combat the spread of AIDS.

"Carbohydrate-binding agents: a potential future cornerstone for the chemotherapy of enveloped viruses?"

Author(s): Balzarini J

Reference: N/A 18(1):1-11.

Published Abstract: Carbohydrate-binding agents (CBAs) inhibit HIV-1 and it is proposed that therapy with such agents may have important implications for the future of anti-HIV therapy. Examples of CBAs include the procaryotic cyanovirin-N (CV-N), plant lectins such as HHA, GNA, NPA, CA and UDA, the monoclonal antibody 2G12 directed against a glycan-containing epitope on HIV envelope gp120, and the mannose-specific non-peptidic antibiotic Pradimicin A, which inhibits the entry of HIV-1 into its target cells. CBAs prevent not only virus infection of susceptible cells, but also inhibit syncytia formation between persistently HIV-infected cells and uninfected lymphocytes. In addition, CBAs may also prevent DC-SIGN-mediated transmission of HIV to T-lymphocytes. Therefore, CBAs qualify as potential **microbicide** drugs. Long-term exposure of HIV to CBAs in cell culture results in the progressive deletion of N-glycans of HIV gp120 in an attempt of the virus to escape drug pressure. In this respect, the CBAs are endowed with a high genetic barrier. Multiple mutations at N-glycosylation sites are required before pronounced phenotypic drug resistance development becomes evident. CBA treatment of HIV may consist of a novel chemotherapeutic concept with a dual mechanism of antiviral action: a direct antiviral activity by preventing HIV entry and transmission to its target cells, and an indirect antiviral activity by forcing HIV to delete glycans in its gp120 envelope. The latter phenomenon will result in creating 'holes' in the protective glycan shield of the HIV envelope, whereby the immune system may become triggered to produce neutralizing antibodies against previously hidden immunogenic epitopes of gp120. If this concept can be proven in *in vivo*, low-molecular-weight non-peptidic CBAs such as Pradimycin A may become the cornerstone for the efficient treatment of infections of those viruses that require a glycosylated envelope (that is, HIV, but also hepatitis C virus) for entry into its target cells. In addition, influenza virus and coronavirus infections may also qualify to be treated by CBAs.

"Microbicides for HIV/AIDS. Electrophoretic fingerprinting of CD4+ T-cell model systems"

Author(s): Fairhurst D, Rowell RL, Monahan IM, et al

Reference: N/A 23(5):2680-7.

Published Abstract: New measurements of the dependence of the surface charge on the pH and electrolyte concentration for three living human white blood cell lines that are the principal targets of the HIV-1 virus are reported. Comparison of the electrophoretic fingerprint (EF) pattern, especially the line of zero mobility, with that of reference colloids establishes the separate individual identities and shows that all three exhibit a zwitterionic surface. With the EF results as a guide, preliminary biological infectivity measurements showed that small polyvalent cations modulate the negative charge on the T-cell surface in a way that strongly affects the infection kinetics. H9 cells were exposed to an infectious virus (X4), and the data showed that HIV interaction with target cells is enhanced by physiological fluids. The nondestructive methodology described is generally applicable to characterization of the surface charge and determination of the colloidal stability of any aqueous charged colloidal system without reference to any model of the double layer.

"Preclinical safety assessments of UC781 anti-HIV topical microbicide formulations"

Author(s): Patton DL, Cosgrove Sweeney YT, Balkus JE, et al

Reference: N/A Epub ahead of print.

Published Abstract: The nonnucleoside reverse transcriptase inhibitor (NNRTI) UC781 is under development as a potential **microbicide** to prevent sexual transmission of the human immunodeficiency virus type 1 (HIV-1). Two gel formulations of UC781 (0.1% and 1.0%) were evaluated in a range of preclinical safety assessments including systemic absorption analysis following topical application in the pigtailed macaque models for vaginally and rectally applied topical **microbicides**. High sensitivity HPLC analysis of serum samples showed that no systemic absorption of UC781 was detected after repeated vaginal or rectal application of either product. However, high levels of UC781 were detectable in the cervicovaginal lavage samples up to 6 hours after product exposure. Both formulations were safe to the vaginal microenvironment, even with repeated daily use, as evidenced by colposcopy, cytokine analysis and lack of impact on vaginal microflora. By contrast, rectal application of 1.0% UC781 formulation caused an increased expression of numerous cytokines not observed after 0.1% UC781 rectal applications. These results provide additional support for the continued development of UC781 formulations as anti-HIV **microbicides**.

"Preclinical testing of candidate topical microbicides for anti-HIV-1 activity and tissue toxicity in a human cervical explant culture"

Author(s): Cummins JE Jr, Guarner J, Flowers L, et al

Reference: N/A Epub ahead of print.

Published Abstract: Objective: A human cervical explant culture was utilized for the preclinical assessment of anti-HIV-1 activity and tissue toxicity of formulated, candidate topical **microbicides**. Products tested included cellulose acetate 1, 2-benzene dicarboxylate (CAP), a carrageenan-based product (PC-515), a naphthalene sulfonate polymer (PRO 2000), a lysine dendrimer (SPL7013), a non-nucleoside reverse transcriptase inhibitor (UC781), and an

antimicrobial peptide (D2A21), along with their placebos. Methods: Cervical explants were cultured overnight with HIV-1 with or without product, washed, and followed for HIV-1 infection. HIV-1 infection was determined by p24gag levels in the basolateral medium and by immunohistochemical analysis of the explant. Product toxicity was measured by the MTT assay and histology. Results: CAP, PRO 2000, SPL7013, and UC781 consistently prevented HIV-1 infection in all explants tested. PC-515 and D2A21 prevented HIV-1 infection in 50% or less of the explants tested. Placebos did not prevent infection in any of the explants tested. With the exception of PRO 2000 (4%), the MTT assay and histological analysis of the other products and placebos showed minimal toxicity to the epithelium and submucosa. Conclusion: Collectively, these data suggest that this culture system can be used for evaluating the safety and efficacy of topical **microbicides** designed for vaginal use.

"Safety, acceptability, and tolerability of 3 topical microbicides among heterosexual Kenyan men"

Author(s): Bukusi EA, Steele M, Cohen CR, et al

Reference: N/A 44(4):423-8.

Published Abstract: OBJECTIVES: To compare the acceptability, tolerability, and safety of 3 topical **microbicide** formulations (62% ethyl alcohol in emollient gel and 0.1% and 0.4% benzalkonium chloride on a sanitary wipe) for use on male genitalia. DESIGN: This triple-randomized crossover study among men attending a sexually transmitted disease (STD) clinic in Nairobi, Kenya assigned individuals without clinical evidence of an STD to apply products to the penis in a predetermined random order, each for a 2-week period with a 1-week washout period between each product. Men recorded side effects and were examined for adverse events. RESULTS: Of 39 participants, 33 (84%) completed 6 clinic visits plus 3 home visits by community health workers. Participants reported use of 62% ethanol gel and 0.1% and 0.4% benzalkonium on 99%, 99%, and 96% of daily scheduled applications; 99%, 98%, and 97% of preintercourse applications, and 99%, 94%, and 98% of postintercourse applications. All participants said they would recommend all 3 products to a friend; 72% preferred the 62% ethanol gel, 17% the 0.1% benzalkonium, and 11% the 0.4% benzalkonium. One person developed objective signs of a genital ulcer after 14 days of 0.4% benzalkonium wipe use. CONCLUSIONS: Two of the 3 topical **microbicides** had minimal reported adverse effects, and no adverse effects were observed during use of the ethanol gel, which was preferred by most men.

"Sex preparation and diaphragm acceptability in sex work in Nairobi, Kenya"

Author(s): Sharma A, Bukusi E, Posner S, et al

Reference: N/A 3(4):261-8.

Published Abstract: BACKGROUND: Women in sex work stand to benefit if the contraceptive diaphragm alone or combined with a **microbicide** proves to be an effective barrier method against HIV and sexually transmissible infection (STI). Currently, contraceptive diaphragm users are advised to leave the diaphragm in situ without concomitant use of other intravaginal substances for at least 6 h after intercourse. METHODS: We conducted in-depth interviews on sexual behaviour including post-coital intravaginal practices with 36 women in sex work and 26 of their clients and held two focus-group discussions, each with 10 women. RESULTS: The women described adapting several potentially harmful substances, such as cloth and soapy water, for post-coital vaginal use to ensure personal hygiene, disease prevention and client pleasure. Some wanted to clean themselves and remove the diaphragm early,

fearing exposure to HIV infection for themselves and their subsequent clients. Clients indicated their desire for 'dry sex', vaginal cleanliness and reduced risk of infection through vaginal cleaning. CONCLUSIONS: The diaphragm as a female-controlled barrier method for HIV/STI prevention may have limited acceptability among women in sex work if its effectiveness depends on a 6-h post-coital wait before removal, along with avoidance of concomitant use of intravaginal substances. In keeping with the beliefs of the the female sex workers and their needs and practices, alternative intravaginal substances and modes of insertion that will not disrupt vaginal flora, injure vaginal epithelium, damage the diaphragm or counteract potentially beneficial effects of **microbicides** are needed. The possibility of removing the diaphragm sooner than the recommended 6 h for contraception should be further studied.

"The search for a topical dual action spermicide/microbicide"

Author(s): Hughes LM, Griffith R, Aitken RJ

Reference: N/A 14(7):775-86.

Published Abstract: There is an urgent clinical need to research novel methods of fertility control that are also protective against sexually transmitted diseases (STDs) such as the human immunodeficiency virus (HIV) or Chlamydia. The most obvious way to generate such a dual-purpose contraceptive method would be to develop safe, effective spermicides that were also active against a wide range of pathogenic organisms. The currently available formulations such as nonoxynol-9, gramicidin and benzalkonium chloride are effective spermicides but are toxic to the vaginal epithelium and do not provide protection against STDs. Over 60 agents are in clinical trials as potentially safer topical spermicides and/or **microbicides**. Compounds that have reached this stage of development include acid buffers, detergents, dendrimers, non-nucleoside reverse transcriptase inhibitors and anionic polymers. In addition, a number of potential spermicides/**microbicides** are the subject of preclinical investigation, including beta-cyclodextrin, cyanovirin, porphyrins, cyclotriazadisulfonamides, dermaseptins, short-interfering RNA (siRNA) and HIV antibodies. The chemical principles underlying these disparate approaches and potential avenues for future investigation are discussed.

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4. PUBLISHED RESEARCH: RELEVANT BASIC AND TRANSLATIONAL SCIENCE

"Reduction of HIV-1 RNA levels with therapy to suppress herpes simplex virus"

Author(s): Nagot N, Ouedraogo A, Foulongne V

Reference: N/A 356(8):790-9.

Published Abstract: BACKGROUND: Epidemiologic data suggest that infection with herpes simplex virus type 2 (HSV-2) is associated with increased genital shedding of human immunodeficiency virus type 1 (HIV-1) RNA and HIV-1 transmissibility. METHODS: We conducted a randomized, double-blind, placebo-controlled trial of HSV suppressive therapy with valacyclovir (at a dose of 500 mg twice daily) in Burkina Faso among women who were seropositive for HIV-1 and HSV-2; all were ineligible for highly active antiretroviral therapy. The patients were followed for 24 weeks (12 weeks before and 12 weeks after randomization). Regression models were used to assess the effect of

valacyclovir on the presence and quantity of genital and plasma HIV-1 RNA and genital HSV-2 DNA during treatment, adjusting for baseline values, and to evaluate the effect over time. RESULTS: A total of 140 women were randomly assigned to treatment groups; 136 were included in the analyses. At enrollment, the median CD4 cell count was 446 cells per cubic millimeter, and the mean plasma viral load was 4.44 log₁₀ copies per milliliter. With the use of summary-measures analysis, valacyclovir therapy was found to be associated with a significant decrease in the frequency of genital HIV-1 RNA (odds ratio, 0.41; 95% confidence interval [CI], 0.21 to 0.80) and in the mean quantity of the virus (log₁₀ copies per milliliter, -0.29; 95% CI, -0.44 to -0.15). However, there was no significant decrease in detection of HIV (risk ratio, 0.93; 95% CI, 0.81 to 1.07). HSV suppressive therapy also reduced the mean plasma HIV-1 RNA level by 0.53 log₁₀ copy per milliliter (95% CI, -0.72 to -0.35). Repeated-measures analysis showed that these effects became significantly stronger during the 3 months of follow-up. CONCLUSIONS: HSV suppressive therapy significantly reduces genital and plasma HIV-1 RNA levels in dually infected women. This finding may have important implications for HIV control.

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5. OTHER PREVENTION APPROACHES

"India to market female condoms"

Date: 15 March 2007

Source: *Indo-Asian News Service*

<http://www.indiaenews.com/health/20070315/43118.htm>

India Wednesday launched a major initiative to introduce female condoms across the country, with an NGO in Tamil Nadu planning a usage study in six districts.

The central government, in collaboration with the Hindustan Latex Ltd and the National Aids Control Organisation (NACO) began a nationwide initiative in October to provide female condoms at just Rs.3 to NGOs working with female sex workers. The government has decided to distribute 500,000 female condoms by June in the first phase at a cost of Rs.180,000 in its second line of defence against HIV/AIDS, said a Tamil Nadu State Aids Control Society (TANSACS) official here. The project will reach out to 11,000 sex workers in the country with the help of 400 civil society groups. The first part of the initiative, to cover 3,000 sex workers, will be completed by the year-end. The scheme is being implemented in eight states simultaneously, with an initial acceptability study done in Tamil Nadu and an operation research study in Gujarat and West Bengal.

TANSACS Wednesday announced that it has acquired 60,000 female condoms and has begun distributing them through six NGOs in Kanyakumari, Madurai, Tiruchirappally, Salem, Vellore and Chennai. "It is for the first time that a government (the Tamil Nadu government) is supporting such a pilot project," TANSACS project director Supriya Sahu told IANS. "We are looking at the reproductive rights of women directly. Most women do not have this right to choose. This is a HIV-AIDS prevention tool under a woman's control," she said. "For the first time, a woman will have a preventive tool in her own hand."

"We will monitor and make public our findings on acceptability, usage and efficacy by April in a report," said Sahu. TANSACS will also reach female condoms to another 800,000 women through self-help groups, she added. A study in the late '90s found 60 percent of sex workers in Tamil Nadu willing to use female condoms.

Each female condom costs Rs.50, but Hindustan Latex has made them available to NACO at a subsidy. NACO will distribute condoms to community health workers in ongoing AIDS prevention programmes among commercial sex workers. The community worker will get one condom at Rs.3 and will be allowed to sell it to the user, a female commercial sex worker, at Rs.5 as there has to be a 30 percent cost recovery for the programme to succeed. NACO is making the condoms available to AIDS control societies in Tamil Nadu, Maharashtra, Andhra Pradesh, Karnataka, Gujarat, West Bengal and Uttar Pradesh.

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6. POLITICS AND POLICY

"HIV/AIDS in India complex, 'overwhelming,' NEJM perspective says"

Date: 15 March 2007

Source: *Kaiser Daily HIV/AIDS Report*

http://www.kaisernetwork.org/daily_reports/rep_index.cfm?DR_ID=43602

HIV/AIDS in India is complex and "overwhelming," national correspondent Robert Steinbrook writes in a *New England Journal of Medicine* perspective. According to Steinbrook, "whatever success" India has in controlling HIV/AIDS will "immediately have an impact on the overall world situation" because India has a large number of HIV-positive people (Steinbrook, *NEJM*, 3/15). According to the "2006 Report on the Global AIDS Epidemic" released in May 2006 by UNAIDS, India has the highest number of HIV-positive people in the world, with 5.7 million people living with the virus. Despite the high number of HIV-positive people in India, the country's HIV prevalence is less than 1% because of its large population (*Kaiser Daily HIV/AIDS Report*, 12/21/06). According to Steinbrook, the UNAIDS report has "served as a wake-up call" to India. Steinbrook writes that Sujatha Rao, director-general of India's National AIDS Control Organization, in January at a conference on HIV/AIDS treatment said, "We have come a long way from complete denial of the HIV epidemic when it was first discovered in 1986 to a complete acceptance of the fact that we have a problem." India in 2006 spent \$129 million on HIV/AIDS services, with the majority of the funding from outside donors, according to Steinbrook. Six of India's 35 states and territories in 2005 recorded a high HIV prevalence; however, only 10% to 20% of HIV-positive people in the country know their status, Steinbrook writes. He adds that commercial sex workers, men who have sex with men, injection drug users and migrant workers are at a high risk of contracting HIV, and the virus also is transmitted vertically and through breast-feeding. According to Steinbrook, HIV prevention efforts in India are "hampered by gaps in knowledge and by cultural, legal and medical factors." Although India is "so populous and complex that it is easy to despair that the task of controlling HIV within its borders is hopeless and overwhelming," the country has "substantial resources" and has been successful in fighting other diseases -- such as polio, smallpox and tuberculosis -- Steinbrook says. He adds that "an effective, multifaceted response" in preventing and treating HIV/AIDS "could avert an even more catastrophic epidemic" (*NEJM*, 3/15).

The perspective is available online at <http://content.nejm.org/cgi/content/full/356/11/1089?query=TOC>. More information about HIV/AIDS in India is available online at <http://www.globalhealthreporting.org/index.asp>.

"The AIDS denialists are still around"

Date: 28 February 2007

Source: *IAS Newsletter*

Author(s): John P. Moore, Jeanne Bergman, Mark A. Wainberg [1]

When AIDS denialists are mentioned to HIV professionals, a common response is the question, "Are these people still around?" Unfortunately, they are indeed still active. Their insistence that HIV either does not exist, or that it is a real but harmless passenger virus, continues to confuse and kill. This is particularly true in South Africa where, since 1999, President Mbeki has taken the AIDS denialists all too seriously.[2,3]

The resulting scientifically flawed policies of the Mbeki administration, including resistance to scaling up the provision of antiretroviral treatment, cost South Africa an uncountable number of HIV infections and deaths during the explosive expansion of the epidemic there in the 1990s and in the first years of the 21st century. Using the 2003 model developed by the South Africa Actuarial Society, HIV prevalence within the adult population is now estimated to be almost 20%. Recently, AIDS activists and scientists, led by the Treatment Action Campaign (TAC), scored a major victory over the beetroot, garlic and lemon juice quackery promoted by South African Health Minister Manto Tshabalala-Msimang. Improved access to antiretroviral drugs (ARVs) to the many South Africans who need them now seems finally to be happening, thanks in no small part to the courageous position taken by the Deputy Health Minister, Nozizwe Madlala-Routledge, who has led the policy shift on HIV in the South African government.[4]

This is an important success, but it will not cause the AIDS denialists to disappear overnight. Their activities are largely, but not exclusively, conducted over the internet on websites that thrive on medical conspiracy theories. The manifest nonsense of what is perpetrated in cyberspace on sites like these is obvious to HIV professionals, but can be highly misleading to the general public, particularly those who are gullible or desperate.

The real-world impact of the arguments made by AIDS denialists is exemplified by an ongoing legal case in Australia. A man convicted for knowingly exposing two women to HIV and infecting one of them is defending himself in the sentencing phase using two classic denialist claims: that HIV does not exist and, even if it were a real virus, it cannot be transmitted heterosexually. The denialist position is represented in court by Valendar Turner and Eleni Papadopoulos-Eleopoulos, staff members of the Royal Perth Hospital who have never worked on HIV themselves.[5,6] Leading Australian HIV scientists have devoted significant time and effort to the trial, acting as expert witnesses. The participation of AIDS scientists is necessary to debunk denialist misinformation in a highly visible venue, irrespective of whether one believes in the merits of imprisonment for sexual behavior such as the defendant's. A similar criminal case is now pending in Canada. There now needs to be international coordination to prevent further waste of professional resources on scientifically unfounded claims.

Another high-profile event will take place in Los Angeles later this year. The Medical Board of California filed an accusation of medical neglect against Dr. Paul Fleiss because his inaction led to the death of a three-year old girl from AIDS. The Attorney General's Office will bring the charges before an Administrative Law Judge later this year. The child's HIV-positive mother, Christine Maggiore, a very active denialist,[7] proselytizes in *Mothering*

Magazine and via the internet against the prophylactic use of ARVs by HIV-positive pregnant women, and in favor of breastfeeding.[8]

Maggiore herself took no precautions against perinatal transmission and would not allow her daughter to be tested for HIV even when she was desperately ill - all because she refuses to accept that HIV is a potentially lethal virus. The child, tragically, did not live long enough to be able to formulate her own opinions. The cause of death, according to a September 15, 2005 report by the Los Angeles County Coroner, was AIDS-related pneumonia.[9] Justice should prevail, but there is always a concern when complex medical and scientific issues about HIV and AIDS are evaluated and applied by laypeople. Substantial media coverage of this trial must be anticipated. The ensuing publicity will increase the likelihood that yet more people will suffer real consequences by acting on misinformation spread by the AIDS denialists.

Roberto Giraldo, one of Maggiore's advisors and a research technician at the New York Presbyterian Hospital, appeared in a documentary film that aired in Latin America last year. In it, he encouraged HIV-infected people to stop taking ARVs and instead follow his advice on "better nutrition" as an AIDS remedy. Mexican community advocates have reported that, since it has aired, over 150 people living with HIV in Mexico City, misled by this documentary's misinformation, have discontinued their antiretroviral treatment, a step which will seriously impair their health if prolonged. Giraldo previously influenced Manto Tshabalala-Msimang's promotion of "natural remedies" for AIDS in South Africa; the AIDS denialists are all inter-connected, and they operate globally.

The links between AIDS denialism and the alternative medicine industry add yet another twist to the story. Matthias Rath is a multi-millionaire businessman whose efforts to promote the sales of his company's micronutrient-based AIDS remedies in South Africa are the subject of a recent exposé in *The New Yorker* by Michael Specter. David Rasnick, an AIDS denialist, was employed by Rath to help conduct illegal "clinical trials" of these micronutrients, the results of which were published in a full-page, very expensive advertisement in *The New York Times* [10]. Similar advertisements in the South African press, urging South Africans with HIV to reject antiviral medications, are no longer permitted as a result of rulings by the Advertising Standards Authority of South Africa (ASASA).[11] Rasnick repeatedly misrepresented himself in the South African press as having a formal affiliation at the University of California, Berkeley; although his eccentric views on HIV/AIDS are similar to those of that university's Professor Peter Duesberg, Rasnick himself has no status there.[12]

Another AIDS denialist with close links to Rath is Anthony Brink, who in January 2007 filed a bizarre complaint of genocide against TAC's founder and current Chair, Zackie Achmat, in the International Criminal Court in The Hague. The indictment alleges that Achmat has poisoned South Africans with ARVs and demands that Achmat be incarcerated, strapped blind-folded to a gurney and forcibly injected with AZT and similar drugs. No doubt the successes of TAC in helping put South African AIDS policies on a rational basis have irked Brink and his fellow AIDS denialists.[13]

In New York City, public policy may soon be changed to exclude children from clinical trials, as a direct result of AIDS denialism. Three years ago, a freelance journalist, Liam Scheff, claimed that foster children with AIDS in a New York City specialized care facility were being abused as experimental guinea pigs and poisoned with ARVs. In fact, the children were participating in National Institutes of Health PACTG (Paediatric AIDS Clinical Trials Group) clinical trials coordinated by Columbia University Medical Center. The trials were designed to determine the most effective

paediatric dosages of drugs already approved for adults with HIV but not available to children. The medications tested included antiretrovirals, immune system stimulators, drugs to prevent the opportunistic infections that can kill immune-compromised children (such as chicken pox) and it also tested interventions to prevent postnatal seroconversion in HIV-exposed infants. Children were enrolled with the consent of parents or guardians and under the oversight of New York City's Administration of Children's Services. Many of these children were African-American, leading to allegations of Tuskegee-style experimentation that prompted local community politicians to become involved without knowing the facts or understanding the science.[14] As a result, a potentially tragic policy change is being contemplated that would exclude foster children from all clinical trials, no matter how urgent the medical emergency. It is ironic that the stunning success of ARVs in paediatric populations seems to have allowed some communities to forget the devastating death rates among HIV-infected children in the 1980s and early 1990s, a situation which drove researchers and physicians to make adult drugs available to children in the first place.

The BBC in 2004 broadcast a video version of Scheff's story, with "research" by the AIDS denialist writer Celia Farber and starring Christine Maggiore. The lurid insinuations were repeated on the BBC website, without any check into the underlying facts. A number of individuals, including the authors of this article, have registered a formal protest with the BBC, identifying many specific errors and misleading claims and noting how this shoddy journalism has damaged public health.[15]

Last spring, *Harper's Magazine* printed a long article by Celia Farber in which she questioned the use of nevirapine to prevent mother-to-child transmission of HIV, despite the astonishing success of the drug in preventing vertical transmission, while lionizing Peter Duesberg, one of the earliest AIDS denialists. Her article repeated many of the scientific errors, innuendo and misconceptions that AIDS denialists usually perpetrate over the internet and has been thoroughly rebutted by scientific experts. Disturbingly, a well-regarded popular science magazine, *Discover*, has now published a long interview/book-plug with Ms Farber.

What can HIV professionals do about the continued activities of the AIDS denialists? First, be aware of efforts to counter their campaign of misinformation. HIV scientists and activists have established a website for this purpose at www.AIDStruth.org. We encourage IAS members to read the information posted on this site and forward the link to friends and colleagues. Background information and supporting documentation for a number of the events and issues covered in this article is available on the website at www.AIDStruth.org/iasnewsletter.

Second, challenge AIDS denialism and all pseudoscience whenever it appears in the legitimate local and national press. For example, HIV professionals might consider whether they wish to support in any way magazines like *Harper's* and *Discover* that give space to AIDS denialists.

Third, if AIDS denialism surfaces within your own institution, particularly if students become involved, bring the weight of your influence and scientific knowledge to rebut its spurious claims.

Finally, serious consideration should be given to the consequences of what the AIDS denialists have done and will continue to do, if unchecked. There are well-accepted limits to free speech when it applies to public health (is it considered acceptable to promote cigarette-smoking in schools?). The denialists will not simply disappear; their motivations (publicity-seeking, profit, personal denial) are too strong. Coordination on an international scale is now required to defeat them wherever they surface. HIV professionals need to know what the denialists' agendas

are, and educate their patients and the public accordingly before the deadly impact of this phenomenon has additional opportunities to expand the AIDS epidemic.

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- 15 The full complaint is available online at www.AIDStruth.org.

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7. ANNOUNCEMENTS

Microbicides 2008 website available

<http://www.microbicides2008.com/>

The **Microbicides 2008** website is now available! The conference will be held in New Delhi, India, from Sunday, 24 February to Wednesday, 27 February 2008. The conference intends to provide updates on the current state and future efforts in **microbicide** research and development in different parts of the world. In addition to basic research and innovative product development of novel **microbicides**, the progress made in areas of ethics, clinical research, socio-behavioral and epidemiological studies, accessibility and acceptability issues will be discussed. A list of hotels at which rooms have been reserved for conference participants is posted on the website. Information on registration, abstract submission, and scholarships will be available soon.

Microbicides Medical Officer (closing date 9 April 2007)

The WHO Department of Reproductive Health and Research (RHR) is the focal point within the United Nations system for research, development, advocacy and promotion of **microbicides** for the prevention of sexually transmitted infections, especially HIV. The Department aims to build capacity in developing country institutions to design, implement and complete clinical safety and effectiveness studies of promising candidate **microbicides**, and develop strategies for acceptable and sustainable product introduction; to sponsor and coordinate selected **microbicide** research projects in collaboration with partners; to strengthen national capacity to oversee **microbicide** research in the context of best practices for HIV prevention research; and, to strengthen developing-country national regulatory authority capacity to oversee clinical trials, review licensure applications and implement appropriate post-licensure monitoring procedures.

RHR is looking for a qualified person to lead WHO's work in this exciting area. For more information, please follow this link: <http://www.who.int/employment/vacancies/en/> and look for vacancy notice HQ/07/RHR/FT237.

Reproductive Health 2007 call for abstracts

Abstract submissions are now being accepted for Reproductive Health 2007. Abstracts demonstrating high quality research practices and relevancy to the meeting objectives will be selected for oral or poster presentation during the scientific session of the meeting. All oral and poster abstracts accepted for scientific presentation will be published in the August 2007 issue of the journal *Contraception, An International Reproductive Health Journal*.

For detailed information on submitting an abstract, visit <http://www.arhp.org/rh2007/2007callforabstracts.cfm>. Also, feel free to contact Shama Alam, ARHP education associate, at (202) 466-3825 or SAlam@arhp.org. For more information about Reproductive Health 2007 please visit www.arhp.org/rh2007 or send an e-mail to conferences@arhp.org.

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