



ALLIANCE FOR MICROBICIDE DEVELOPMENT

25 July 2008, Volume 9, Number 29

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

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

Its purpose is to:

- Raise awareness around the broadest possible range of opinions and information about microbicides disseminated in scientific journals and the media; and
- Provide an objective basis for decision-making and evidence-informed advocacy.

Articles included in the Digest do not necessarily reflect the views of the Alliance. No press releases are included, however when information from a press release is picked up by the media, that coverage is included. To suggest material for inclusion, please contact digest@microbicide.org.

The Digest is produced in a web-based format. Readers can view complete issues of the Digest or search by keyword for individual articles at http://www.microbicide.org/cs/weekly_news_digest. If you would like to be removed from the Digest distribution list, please send an email to 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

Alliance Initiates Work Toward a Topical Product Inventory: Regulated and Unregulated Lubricants and Spermicides

www.microbicide.org

The Alliance is initiating work toward a comprehensive inventory of topical lubricating products, including spermicides, that are on the US domestic and international markets. This inventory will seek to include detailed information on regulated products, such as those available over-the-counter (OTC) and by prescription, with ingredients and safety (preclinical and clinical) data where available. All unregulated products will be compiled by country in a separate list, and distributors will be contacted for follow-up information.

Please contribute! To help in this work, we are seeking information from all advocates, agencies, countries, developers, and researchers. To supply information, please send any and all details (such as product name, website, ingredients, manufacturer contact information, etc.) to Stephanie Tillman at stillman@microbicide.org. When available, please also fax or mail product labels, boxes, and flyers to 301-588-8390 or our address below. We appreciate any information you can provide.

To note: We have received feedback that in countries where clinical trials of candidate **microbicides** have taken place, there are products on the market with names similar to those being tested. If you are aware of these products, please send this information to the Alliance, who will include it in the inventory and bring it to the attention of appropriate agencies.

Thanks for your support! We look forward to publicly providing this information once the inventory is substantially complete.

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2. MEDIA COVERAGE OF MICROBICIDES

"Africa: Researchers to prove ARVs effectiveness"

Date: 24 July 2008

Source: *The Monitor*

Author(s): Kakaire A Kirunda

<http://allafrica.com/stories/200807231245.html>

Researchers have initiated studies to establish whether antiretroviral drugs can effectively be used to block HIV infection. Scheduled to end at the close of next year, the study is now recruiting participants and will initially start in the US, with additional sites soon opening in Uganda and South Africa.

According to the **Microbicide** Trials Network (MTN), the ARV drug tenofovir has particular promise because it can be formulated as either an oral tablet or a **vaginal gel** to be used daily. This will be the first clinical trial to directly compare the tablet and **vaginal gel** formulations of tenofovir, amid scientific and practical challenges.

A statement issued last week by MTN notes that because certain cells in the vagina are easy targets for the virus, women are more than twice as likely as their male partners to acquire HIV through sexual intercourse.

As such, "the clinical study, known as MTN-001, seeks to understand how each formulation of tenofovir works in these infection-prone cells, information that will help researchers determine the optimal doses needed to achieve drug concentrations most likely to prevent HIV in women."

This development comes at a time when HIV prevention efforts have suffered serious blows over the last one year that saw two promising trials of candidate **microbicides** and vaccines stopped. In early 2007, a trial of the gel meant to prevent HIV infection in women was prematurely called off after researchers found that it did not protect the women from infection.

Then late 2007 saw the stoppage of the vaccine trial because although the candidate vaccine did not cause any infections, it made participants vulnerable to HIV infection.

This has since led to writing off of another vaccine trial dubbed PAVE 100 in which Ugandan participants were to be enrolled. However, the Principal Investigator of the IAVI (International Aids Vaccine Initiative Vaccine) Programme in Uganda Dr Pontiano Kaleebu said on Tuesday that all was not lost.

"We are just being cautious. The large scale studies will not be done, but what is going to happen is that smaller PAVE 100 trials will go on in the US," Dr Kaleebu said. "And there are several other vaccine trials going on around the world involving different vaccines. So the search is still on."

An estimated one million people are living with HIV/Aids in Uganda while hundreds get infected every year, according to Health officials.

EDITOR'S NOTE: *Another media write-up of MTN-001 is available at*

http://www.wkyc.com/news/news_article.aspx?storyid=93281

"Gates Foundation's CEO looks back - and ahead"

Date: 24 July 2008

Source: *The Chronicle of Philanthropy*

Author(s): Caroline Preston

Twelve weeks into her job as a consultant to a Hollywood film company, Patty Stonesifer knew she'd made a mistake. Her mind kept wandering to a fledgling foundation started by her former boss at Microsoft, Bill Gates, and his wife, Melinda, to bring computers to public libraries.

Nearly 12 years later, Ms. Stonesifer is stepping down as chief executive of that start-up philanthropy, after overseeing its growth into the nation's largest and most visible foundation. The Bill & Melinda Gates Foundation, which was formed in 2000 from a merger between the Gates Learning Foundation and a philanthropy run by Mr. Gates's father, William H. Gates Sr., has \$38-billion in assets and will give out more than \$3-billion next year. The foundation now has 550 employees, and that number is expected to nearly double in the next few years, to more than 1,000.

But Ms. Stonesifer, the sixth of nine children -- whose father started a food pantry to serve the north side of Indianapolis -- doesn't intend to step away from the foundation altogether. She's considering whether to oversee a new grant-making project at the Gates fund.

Her departure from the top job caps a major transition. Bill Gates retired from full-time work at Microsoft last month to spend more time on philanthropy. And Jeffrey S. Raikes, a Microsoft executive, will take over as chief executive in September.

Ms. Stonesifer has won praise over the years for recruiting talented leaders, maintaining the foundation's focus as it has grown, and emphasizing ways to ensure its dollars make a difference. What's more, she brought a sense of humility to the job, says Vartan Gregorian, president of the Carnegie Corporation of New York.

"Gates could easily have become the 800-pound gorilla, but with Patty at the helm there was never any talk of which foundation is the greatest, only how can we speak on behalf of the 1.4 million nonprofits."

Observers say Ms. Stonesifer's longstanding relationship with the Gateses -- she joined Microsoft in 1987 and oversaw the team on which Ms. Gates worked -- has benefited the foundation greatly.

"One of Patty's biggest strengths has been her knowledge of Bill and Melinda and her ability to, as she used to say, channel them," says Richard D. Klausner, the foundation's former director of global health.

"That's enabled the foundation to really evolve to reflect their aspirations."

Debates About Results

As the Gates foundation has ballooned in size, however, it has increasingly drawn fire from people inside and outside the nonprofit world. Its spending on global health, for example, has been criticized for emphasizing the development of new vaccines at the expense of the delivery of life-saving medicines and building grass-roots support for preventing the spread of diseases.

In February, a senior official at the World Health Organization accused the Gates foundation of stifling competition among malaria researchers and exerting too much influence over the U.N. body.

For her part, Ms. Stonesifer says the foundation has consistently awarded grants designed to make a major difference in solving problems. "I think we've made the right choices," she says.

The long-term nature of the foundation's goals and the complexity of the problems it has chosen to tackle, however, have made clear-cut successes hard to achieve. "We're very optimistic about the short-term milestones in some programs, and we're very sober about the short-term outcomes in others," she says.

"We'd hoped by now that we'd have a **microbicide** for AIDS, but the early trials have been very disappointing."

Sitting for an interview in the foundation's headquarters along Seattle's Lake Union, Ms. Stonesifer, who took no salary for her work at the Gates fund after earning significant wealth at Microsoft, describes her education in how to use philanthropic dollars effectively. As head of the Gates Learning Foundation until 2000, she oversaw giving to a cause she knew well: using technology to empower people.

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EDITOR'S NOTE: *The full text of this article is available with a subscription at the above website.*

"Meharry testing barrier to HIV"

Date: 22 July 2008

Source: *The Tennessean*

Author(s): Colby Sledge

<http://www.tennessean.com/apps/pbcs.dll/article?AID=/200807220210/NEWS07/807220345>

In a state-of-the-art lab in an unassuming building in North Nashville, Dr. James Hildreth works to achieve a truce with the devastating disease he has been battling for 15 years.

Not a victory. A truce.

Hildreth leads the Center for AIDS Health Disparities Research at Meharry Medical College, where he is developing a cream that could potentially block the transmission of HIV during sex.

The cream could give hope to millions of women in Africa who have no way of protecting themselves from HIV transmission, as well as black women in the United States who are disproportionately affected by the disease.

The vaginal cream, described as a "chemical condom," relies on a sugar found in toothpaste and mouthwash to remove cholesterol the HIV virus needs to spread. The cream is odorless and is designed to be undetectable to a woman's sexual partner.

"In many parts of the world, women are not in the position to negotiate how sex is practiced," including the use of condoms, Hildreth said. "We have been trying to formulate something transparent to the act of having sex. Women might be able to use it without getting permission or even letting the men know they are using it."

Earlier this summer, Hildreth traveled to Lusaka, Zambia, to see how women and men reacted to the feel and the smell of the cream. About 1.1 million Zambians, 17 percent of the adult population, were living with HIV in 2005, according to the United Nations.

Researchers expected men to reject the cream, but most accepted it.

"Even among the most rural of Africans now, the word is starting to get out about what a serious and expansive problem the AIDS pandemic is," Hildreth said. "There's a certain desperation that people feel for something to protect themselves."

Gap is increasing

Meharry received a \$10 million grant from the National Institutes of Health in 2003 to fund AIDS research in a new facility that opened in April of this year. There, in a secure lab, Hildreth and six researchers work with potent strains of HIV.

The research is particularly important to Meharry, one of only four historically black medical institutions in the country, given the disproportionate affect of AIDS on the black U.S. population. Although African-Americans make up 13 percent of the U.S. population, they account for 50 percent of AIDS cases in the

country.

And the gap in Tennessee is growing. In 2006, 660 black residents were diagnosed with AIDS, up from 621 in 2002. During that same period, AIDS diagnoses of white Tennesseans decreased from 357 to 295. Reasons for the disparity vary. Poverty and lack of access to health care are often given as underlying causes, but Meharry researchers are also looking at genetic predispositions that might make black victims more susceptible to contracting the virus and the severity of its symptoms.

They are particularly concerned about black women, who were diagnosed with AIDS at a rate 23 times higher than that of white women in 2005, according to the Centers for Disease Control and Prevention. "African-American women are shouldering the brunt of HIV in the United States, and it has significant implications for the stability of the black family," said Dr. Wayne Riley, Meharry president and CEO.

Work at the Meharry center has taken on even greater significance as the search for an AIDS vaccine has suffered recent defeats. U.S. health officials canceled a large vaccine trial Thursday after two similar tests in September 2007 failed to show any promise in preventing HIV infection or slowing the disease for those who later became infected.

Hildreth's cream has already proved effective with monkeys and mice, and he hopes to receive approval from the Food and Drug Administration this fall to begin the first trials on people early next year.

About 25 Middle Tennessee women and 100 Zambian women would receive the cream to test for reactions to prolonged use. If everything falls into place, the cream would be available in five years.

"It has the potential of being a new target," said Jim A. Turpin, a program officer in the AIDS division of the National Institute of Allergy and Infectious Diseases. "James Hildreth has a lot of very nice data. ... The question becomes, can you do this safely in women?"

Group proud of effort

Hildreth readily acknowledges that there is a chance that the cream, also known as a **microbicide**, could fail. Last year, the final trials of a **microbicide** were halted after tests showed women who used the gel were actually contracting HIV at a higher rate than those using a placebo.

If Hildreth's cream works, it could become one of several drugs used to combat HIV prevention. The goal is to create bundles of treatments that could be personalized, Turpin said.

But Hildreth is not seeking to totally stop the disease. He's just trying to find a way to slow it down.

"At the end of the day, this **microbicide** may not work," Hildreth said. "All the evidence is to the contrary, that it will work, but we do experiments and medical trials to get the answers.

"I do think that just the process of doing it well and trying to be excellent in what we do will make a difference. We think there's layers and layers of significance in what we're doing, and we're very proud to be doing it."

"Crab soup for the soul"

Date: 21 July 2008

Source: *The Statesman (India)*

<http://www.thestatesman.net/page.news.php?clid=25&theme=&usrssess=1&id=214522>

A piece of paper and a tube were handed out to all before ushering the crowd into Max Mueller Bhavan's auditorium. We were urged to punch a hole in the centre of it with the forefinger and view the ensuing performance through it. The exercise, of course, was a matter of choice. On the tube was printed "This is

not a hair gel". I would have loved to believe it was crab gel!

The Creative Art's Crab Soup ~ staged at Max Mueller Bhavan ~ written by Arthur Cardozo and directed by Ramanjit Kaur, was laden with symbols. Each act on stage had more to what was visible. The play had multiple layers sifting through which gave every member in the audience a different perspective.

The play starts with a happy urban couple recalling the days of youth and vigour. Anu, the wife, gives Naru's stories of encouragement a patient hearing. He had been an athlete and thought of nothing but securing pole position. Physical exhaustion has always been a trivial issue for Naru. But now those days seem far away. Anu, the only earning member in the family, finds it difficult to make ends meet with rising medical bills. Naru has been tested HIV positive.

Crab Soup contains several jokes Naru cracks about the Eliza Test. He just couldn't come to terms with the fact that he is an easy target. He is preoccupied with himself and dismisses every indication of the illness. In another scene we find him convincing himself that he was all right. He even finds the mutton curry infected! The play focuses on the emptiness in Anu's life, the vacuity she is so scared of. Caressing a doll that belongs to Choti (her maid), she discovers her craving for motherhood, which she couldn't risk being married to a HIV-positive husband.

This is when an announcement is made about the "crab gel", a contraceptive for women. The play tries to portray the extent Naru would go to turn a blind eye towards his illness. He considers the gel a threat to his manhood. For Anu, the gel gave her protection. She conceives Manu's (her colleagues) child to fulfil her desire to be a mother. Naru never forgets to ask Anu to wear sindoor, for that symbolises marriage, but doesn't bother to ask about the gel!

Excellent work in every department ~ state setting, light design and music ~ ensured a successful play. More than the storyline, credit goes to The Creative Arts for presentation. Symbolism formed the heart of Crab Soup.

Every image highlighted aspects of a relationship that was constantly changing ~ shreds of newspapers were shreds of a torn life the couple were living and long shots of the bathroom stood for the act of washing (Naru of the virus and Anu of moral baggage of having slept with his colleague). But there were times when symbolism marred the flow of script. The actors ~ Anu (Taranjit Kaur), Naru (Vajinder Kumar), Choti (Payal De) and Manu (Souptik Chakraborty) ~ were brilliant, making the hour last forever.

Crab Soup is the result of a series of workshops, research and interviews of HIV positive patients. Forming the backdrop was the research project of NIRRH Bombay, which is working on a **microbicide** extracted from the Indian mud crab.

The director said that HIV was an overdone subject but the crab gel provided hope. The play lacked strength as far as storyline was concerned. But the theme of women's empowerment was always highlighted, even in the last scene when Anu informs Naru of the unborn child.

The concept was innovative but the execution could have been better. Yet, Crab Soup was worth watching.

"CWRU tests HIV treatment for women"

Date: 18 July 2008

Source: *WKYC.com (Cleveland, OH)*

http://www.wkyc.com/news/local/news_article.aspx?storyid=93281&catid=3

A first-of-its-kind clinical research trial at the Case Western Reserve University/University Hospitals AIDS Clinical Trials Unit will look at two different methods of female-controlled HIV prevention: **microbicides** and pre-exposure prophylaxis.

The ground-breaking trial offers women living in the Greater Cleveland area a unique opportunity to help alter the course of the worldwide AIDS epidemic. The clinical trial is the first to be offered through the newly established National Institute of Health-funded **Microbicide** Trials Network.

The development of female-controlled HIV prevention methods are a research priority around the world, as the number of HIV-infected women continues to increase dramatically. Of the estimated 33.2 million people infected with HIV globally, 15.4 million are women.

This trial will investigate the use of **microbicides** as a new method focused on the women's control of their own preventative medicine. **Microbicides** are topical treatments in the form of a gel, foam, cream, or depot device that could decrease or prevent the sexual transmission of HIV. Pre-exposure prophylaxis (PrEP) refers to taking oral medicine prior to sexual activity.

The most effective method currently available for the prevention of HIV infection is the consistent use of condoms. However, research has shown that many women do not have the power to require their husbands or male partners to wear a condom. This is especially true in the developing world, but is also true in economically developed countries such as the United States.

Effective **microbicides** and/or PrEP will allow a woman to take control over her own protection from HIV, rather than having to rely on her male partner to wear a condom. There are no commercially available HIV **microbicides** or PREP medicines available at this time.

This study is enrolling healthy, sexually active, HIV-negative women, age 18-45.

"Because MTN001 is an earlier phase trial, we are not seeking women who are at high risk for HIV infection," said Robert Salata, M.D., Chief, Division of Infectious Diseases and HIV Medicine, University Hospitals, and Co-Principal Investigator of the Case Western Reserve University/University Hospitals AIDS Clinical Trials Unit. "The trial is looking at the acceptability of the **microbicide** and PREP drug to the participants and their adherence in using them over a period of time. We are seeking women who are motivated by their wish to empower women to protect themselves from HIV, and who are able to meet the time and effort requirements of the clinical trial."

The MTN001 trial encourages all those interested in this landmark research to contact the Case Western Reserve University/University Hospitals AIDS Clinical Trials Unit. The trial will last approximately 21 weeks, with 12 clinic visits during that period of time. Compensation is provided to participants. All clinic visits will be at the Clinical Trials Unit site at University Hospitals.

To call to enroll or for more information on HIV **microbicide** trials in Cleveland, call 216.844.AIDS (2437) or go to www.clevelandactu.org.

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3. PUBLISHED RESEARCH: MICROBICIDE-SPECIFIC

"Whither or wither microbicides?"

Author(s): Grant RM, Hamer D, Hope T, et al

Reference: Science. 25 July 2008;321(5888):532-34.

<http://www.sciencemag.org/cgi/content/abstract/321/5888/532>

Published Abstract: After disappointing results from all efficacy trials conducted to date, the field of microbicides research now faces substantial challenges. Poor coordination among interested parties and the choice of nonvalidated scientific targets for phase III studies have hampered progress and created mistrust about the use of microbicides as a method to prevent HIV-1 sexual transmission. Although new promising strategies are available, there will need to be serious reappraisals of how decisions are made to advance the next generations of candidates into clinical trials, and the use of appropriate animal models in this process will be critical.

"Tropism-independent protection of macaques against vaginal transmission of three SHIVs by the HIV-1 fusion inhibitor T-1249"

Author(s): Veazey SR, Ketas AT, Klasse JP, et al

Reference: Proc Natl Acad Sci USA. 22 July 2008;Epub ahead of print.

<http://www.pnas.org/content/early/2008/07/22/0802666105.abstract?maxtoshow=&HITS=5&hits=5&RESULTFORMAT=&andorexacttitle=and&andorexacttitleabs=and&fulltext=microbicide%252C+microbicides&andorexactfulltext=or&searchid=1&usestrictdates=yes&resourcetype=HWCI>

Published Abstract:

We have assessed the potential of the fusion inhibitory peptide T-1249 for development as a vaginal **microbicide** to prevent HIV-1 sexual transmission. When formulated as a simple gel, T-1249 provided dose-dependent protection to macaques against high-dose challenge with three different SHIVs that used either CCR5 or CXCR4 for infection (the R5 virus SHIV-162P3, the X4 virus SHIV-KU1 and the R5X4 virus SHIV-89.6P), and it also protected against SIVmac251 (R5). Protection of half of the test animals was estimated by interpolation to occur at T-1249 concentrations of 40–130 nM, whereas complete protection was observed at 0.1–2 mM. *In vitro*, T-1249 had substantial breadth of activity against HIV-1 strains from multiple genetic subtypes and in a coreceptor-independent manner. Thus, at 1 nM in a peripheral blood mononuclear cell-based replication assay, T-1249 inhibited all 29 R5 viruses, all 12 X4 viruses and all 7 R5X4 viruses in the test panel, irrespective of their genetic subtype. Combining lower concentrations of T-1249 with other entry inhibitors (CMPD-167, BMS-C, or AMD3465) increased the proportion of test viruses that could be blocked. In the PhenoSense assay, T-1249 was active against 636 different HIV-1 Env-pseudotyped viruses of varying tropism and derived from clinical samples, with IC₅₀ values typically clustered in a 10-fold range 10 nM. Overall, these results support the concept of using T-1249 as a component of an entry inhibitor-based combination **microbicide** to prevent the sexual transmission of diverse HIV-1 variants.

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"Enhancement of HIV infection by cellulose sulfate"

Author(s): Tao W, Richards C, Hamer D

Reference: AIDS Res Hum Retroviruses. 15 July 2008;Epub ahead of print.

<http://www.ncbi.nlm.nih.gov/pubmed/18627218>

Published Abstract: Cellulose sulfate, a polyanionic compound derived from cotton, has been proposed as a topical **microbicide** to reduce the sexual transmission of HIV. However, a phase III clinical trial of a **vaginal gel** formulation of cellulose sulfate (Ushercell) had to be prematurely closed after early data indicated **microbicide** users had a higher rate of HIV infection than women using a placebo. The unexpected results of the cellulose sulfate trial prompted us to reexamine and attempt to replicate the available preclinical data for this compound and other polyanions. We show here that cellulose sulfate has a biphasic effect on HIV infection in vitro: at high concentrations it inhibits infection but at low concentrations it significantly and reproducibly increases HIV infection. This stimulatory effect is evident for the R5-tropic strains of virus responsible for sexual transmission, reflects the rate of infection rather than viral growth, and occurs at clinically relevant concentrations of the compound. An examination of published studies shows that the biphasic effect of cellulose sulfate was evident in previous research by independent laboratories and is also found for other polyanions such as dextrin sulfate and PRO2000. These data help in understanding the failure of the Ushercell clinical trial and indicate that cellulose sulfate is not safe for mucosal application in humans.

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4. PUBLISHED RESEARCH: RELEVANT BASIC AND TRANSLATIONAL SCIENCE

"Duffy antigen receptor for chemokines mediates trans-infection of HIV-1 from red blood cells to target cells and affects HIV-AIDS susceptibility"

Author(s): He W, Neil S, Kulkarni H, et al

Reference: Cell Host and Microbe. 17 July 2008;4:52-62.

<http://www.cellhostandmicrobe.com/content/article/fulltext?uid=PIIS193131280800190X>

Published Abstract: Duffy antigen receptor for chemokines (DARC) expressed on red blood cells (RBCs) influences plasma levels of HIV-1-suppressive and proinflammatory chemokines such as CCL5/RANTES. DARC is also the RBC receptor for *Plasmodium vivax*. Africans with *DARC 46C/C* genotype, which confers a DARC-negative phenotype, are resistant to *vivax* malaria. Here, we show that HIV-1 attaches to RBCs via DARC, effecting *trans*-infection of target cells. In African Americans, *DARC 46C/C* is associated with 40% increase in the odds of acquiring HIV-1. If extrapolated to Africans, 11% of the HIV-1 burden in Africa may be linked to this genotype. After infection occurs, however, DARC-negative RBC status is associated with slower disease progression. Furthermore, the disease-accelerating effect of a previously described *CCL5* polymorphism is evident only in DARC-expressing and not in DARC-negative HIV-infected individuals. Thus, DARC influences HIV/AIDS susceptibility by mediating *trans*-infection of HIV-1 and by affecting both chemokine-HIV interactions and chemokine-driven inflammation.

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EDITOR'S NOTE: The full text of this article is available for public access at the above website. A media write-up of this article is available at https://www.economist.com/science/displaystory.cfm?story_id=11745521

"Roles of clinical and subclinical reactivated herpes simplex virus type 2 infection and human immunodeficiency virus type 1 (HIV-1)-induced immunosuppression on genital and plasma HIV-1 levels"

Author(s): Nagot N, Ouedraogo A, Konate I, et al

Reference: J Infect Dis. 15 July 2008;198(2):241-49.

<http://www.ncbi.nlm.nih.gov/pubmed/18593294>

Published Abstract: Background. Few longitudinal studies have described the interactions between reactivation of herpes simplex virus type 2 (HSV-2) infection (hereafter, "HSV-2 reactivation") and genital and systemic replication of human immunodeficiency virus type 1 (HIV-1). Methods. Women in Burkina Faso who were seropositive for both HIV-1 and HSV-2 were enrolled in a randomized placebo-controlled trial of therapy to suppress reactivation of HSV-2 infection (hereafter, "HSV suppressive therapy"). During the baseline phase, 6 enriched cervicovaginal lavage specimens were obtained over 12 weeks to detect and quantify the HIV-1 RNA and HSV-2 DNA loads. Results. Women with genital ulcer disease (GUD) detected at least once were more likely than women in whom GUD was not detected (risk ratio [RR], 1.23; 95% confidence interval [CI], 1.09-1.37) to have genital HIV-1 RNA detected during ≥ 1 visit. Similarly, women with genital HSV-2 DNA detected during ≥ 1 clinic visit were more likely than women in whom genital HSV-2 DNA was not detected (RR, 1.17; 95% CI, 1.01-1.34) to have genital HIV-1 RNA detected at least once. In addition, the mean genital HIV-1 RNA loads for women with GUD detected during ≥ 1 visit and women with HSV-2 genital shedding detected during ≥ 1 visit were greater than that for women in whom genital HSV-2 DNA or GUD was never detected. The plasma HIV-1 RNA load was increased among women for whom ≥ 1 visit revealed GUD (+0.25 log(10) copies/mL; 95% CI, -0.05-0.55) or genital HSV-2 DNA (+0.40 log(10) copies/mL; 95% CI, 0.15-0.66), compared with women who did not experience GUD or HSV-2 genital shedding, respectively. The association of HSV-2 reactivations on HIV-1 replication tended to be stronger in patients with a higher CD4(+) cell count (i.e., >500 cells/ μ L). The contribution of HSV-2 to HIV-1 replication among women with CD4(+) cell count of ≤ 500 cells/ μ L was reduced because almost all experienced HIV-1 genital shedding. Conclusions. Both clinical and subclinical HSV-2 reactivations play a role in increasing the rate of HIV-1 replication. HSV suppressive therapy is a promising tool for HIV control. Initiation of such therapy when the CD4(+) cell count is >500 cells/ μ L deserves further investigation. Clinical trials registration. The ANRS 1285 Study is registered with the National Institutes of Health (registration number NCT00158509).

EDITOR'S NOTE: A media write-up of this article is available at

<http://www.aidsmap.com/en/news/9CDFF84B-D737-423B-8419-F68CEF71D678.asp>.

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5. PUBLISHED RESEARCH: RELEVANT BEHAVIORAL AND SOCIAL SCIENCE AND EPIDEMIOLOGY

"Epidemiology of male same-sex behaviour and associated sexual health indicators in low- and middle-income countries: 2003-2007 estimates"

Author(s): Cáceres CF, Konda K, Segura ER, et al

Reference: Sex Transm Infect. 01 August 2008;84Supplement 1

http://sti.bmj.com/cgi/content/abstract/84/Suppl_1/i49?maxtoshow=&HITS=5&hits=5&RESULTFORMAT=&andorexacttitle=&andorexacttitleabs=&andfulltext=microbicide%2C+microbicides&andorexactfulltext=or&searchid=1&usestrictdates=yes&resourcetype=HWCIT&ct

Published Abstract: Objectives: To conduct a systematic review of published and unpublished data from research and public health information systems on the prevalence of male-to-male sex in the total male population; as well as among men who have sex with men (MSM), data on prevalence of heterosexual activity and heterosexual unions; prevalence of condom use with male and female partners; and prevalence of HIV infection and other sexually transmitted infections (STIs). Methods: Key indicators were defined (a) among men in the general population: prevalence of sex with a man ever and last year; (b) among MSM: prevalence of heterosexual experiences ever and last year; proportion of male-female transgenders; proportion of sex workers; prevalence of HIV and other STIs, condom use in last sexual encounter; consistent condom use with men last year; never used a condom with a man. With help from key informants, study searches were conducted in Pubmed, LILLACS, institutional databases, conference records and other sources. Methodology and quality of information were assessed, and the best data available for 2003–7 were selected. Indicator estimates from each study were used to propose regional estimate ranges. Results: A total of 83 new entries were entered into the database in addition to the previous 561, totalling 644. Of these, 107 showing 2003–7 data were selected. Many new studies came from sub-Saharan Africa, portraying hidden HIV epidemics among MSM. The most frequently reported estimate was HIV infection, with high estimate ranges in most of the regions, except for Middle East and North Africa and Eastern Europe. The next most frequently reported was lifetime frequency of heterosexual sex, showing that roughly 50% of MSM ever had sex with a woman. The small number of newer studies reporting prevalence of "sex with a man in last 12 months" between 2003 and 2007, did not warrant enough new evidence to revise our 2005 size estimates for MSM populations. Conclusions: A considerable number of new studies with estimates of relevance to understanding sexual behaviour and HIV among MSM were identified, with an encouraging amount of new data coming from sub-Saharan Africa. However, limitations in the quality, utility and comparability of available information persist. At least three measures could be promoted for use in surveillance and academic studies: standardised indicators for MSM studies; standardised operational definitions of, and instructions to describe, variables; and standardised research designs and data gathering strategies. A prerequisite for this all is intense advocacy to ensure a social climate in which research into such matters is prioritised, resources are made available as needed and the human rights of MSM are respected.

"Estimating the number of HIV infections averted: an approach and its issues"

Author(s): Heaton LM, Komatsu R, Low-Beer D, et al

Reference: Sex Transm Infect. 01 August 2008;84Supplement 1

http://sti.bmj.com/cgi/content/abstract/84/Suppl_1/i92?maxtoshow=&HITS=5&hits=5&RESULTFORMAT=&andorexacttitle=&andorexacttitleabs=&andfulltext=microbicide%2C+microbicides&andorexactfulltext=or&searchid=1&usestrictdates=yes&resourcetype=HWCIT&ct

Published Abstract: Objective: To propose a methodology to estimate the number of new HIV infections averted. Knowledge of HIV infection has increased tremendously and modelling tools to project current

epidemics into the future have greatly improved. Different types of models can be used to estimate HIV infections averted, although the number of new HIV infections averted cannot be measured directly. Method: Using cohort-component population projections, a disease modelling-based approach was used to compare the observed epidemiology of a disease after programme initiation with an expected epidemiology from past trends before programme initiation. The concept of modelling infections averted in a disease modelling-based approach involves a comparison between an "expected" or baseline epidemic with an "estimated" one. A hypothetical example was featured in order to demonstrate the proposed methodology. Using both the Estimation and Projection Package (EPP) and the Spectrum demographic modelling program, the underlying annual incidence levels implied by both the baseline and estimated epidemics were examined. Results: The difference between baseline and estimated incidence levels is interpreted as "infections averted". Strengths and limitations of the approach are discussed. Conclusions: In this study an expected epidemiological approach was compared to one based on observation. Once sufficient data become available, the validation of various country data including HIV prevalence, mortality, and behaviour must be done. Additional information related to behaviour change may be critical to further support arguments for a change in disease trend. It is therefore important to use all available data, consequently strengthening findings from a disease modelling-based approach on HIV infections averted.

"Factors associated with self-reported unprotected anal sex among male sex workers in Mombasa, Kenya"

Author(s): Geibel S, Luchters S, King'ola N, et al

Reference: Sex Transm Dis. 01 August 2008;35(8):746-52.

<http://www.stdjournal.com/pt/re/std/abstract.00007435-200808000-00007.htm;jsessionid=LL0FJyIpP5Lpp44h9S2xbyTgKLscl9yzmB6TzHnPLhJgX4n9gYyN!523807009!181195628!8091!-1>

Published Abstract: Objectives: To identify social and behavioral characteristics associated with sexual risk behaviors among male sex workers who sell sex to men in Mombasa, Kenya. Methods: Using time-location sampling, 425 men who had recently sold, and were currently willing to sell sex to men were invited to participate in a cross-sectional survey. A structured questionnaire was administered using handheld computers. Factors associated with self-reported unprotected anal sex with male clients in the past 30 days were identified and subjected to multivariate analysis. Results: Thirty-five percent of respondents did not know HIV can be transmitted via anal sex, which was a significant predictor of unprotected anal sex [adjusted odds ratio (AOR) 1.92; 95% confidence interval (95% CI), 1.16-3.16]. Other associated factors included drinking alcohol 3 or more days per week (AOR, 1.63; 95% CI, 1.05-2.54), self-report of burning urination within the past 12 months (AOR, 2.07; 95% CI, 1.14-3.76), and having never been counseled or tested for HIV (AOR, 1.66; 95% CI, 1.07-2.57). Only 21.2% of respondents correctly knew that a water-based lubricant should be used with latex condoms. Conclusions: Male sex workers who sell sex to men in Mombasa are in acute need of targeted prevention information on anal HIV and STI transmission, consistent condom use, and correct lubrication use with latex condoms. HIV programs in Africa need to consider and develop specific prevention strategies to reach this vulnerable population.

"Separation of spouses due to travel and living apart raises HIV risk in Tanzanian couples"

Author(s): Vissers DC, Voeten H, Urassa M, et al

Reference: Sex Transm Dis. 01 August 2008;35(8):714-20.

<http://www.stdjournal.com/pt/re/std/abstract.00007435-200808000-00002.htm;jsessionid=LL0MGNtsWjlzrSJ1wzvFT5TnpNhq41zCnTD2T6SvvxrcsWV13qLp!1629792715!181195629!8091!-1>

Published Abstract: Background: Persons with absent partners may be more vulnerable to risky sexual behavior and therefore HIV. Partner absence can be due to traveling (e.g., family visits or funerals) or to living apart (e.g., work-related or in polygamous marriages). We investigated to what extent partner absence leads to more risky sexual behavior in Tanzanian couples. Methods: We compared 95 men and 85 women living apart with 283 men and 331 women living together. Only persons who were still married were included, either living apart or cohabiting at the time of the interview. Subjects were classified into 4 groups: coresidents being either nonmobile or mobile, and people living apart either frequently or infrequently seeing each other. Results: Most people living apart were polygamously married. Men living apart did not report more extramarital sex than coresident men. However, among coresident men, extramarital sex was reported by 35% of those being mobile compared with 15% of those nonmobile. Among women, those living apart reported extramarital sex more often than coresidents (14% vs. 7%), and this was mainly due to women living apart who infrequently saw their husbands. Conclusions: Risky sexual behavior occurs more often in mobile coresident men, and in women living apart infrequently seeing their spouses. These groups are relatively easy to identify and need extra attention in HIV prevention campaigns.

"Willingness of men who have sex with men (MSM) in the United States to be circumcised as adults to reduce the risk of HIV infection"

Author(s): Begley EB, Jafa K, Voetsch AC, et al

Reference: PLoS One. 16 July 2008;3(7):e2731.

<http://www.plosone.org/article/info%3Adoi%2F10.1371%2Fjournal.pone.0002731>

Published Abstract: Background Circumcision reduces HIV acquisition among heterosexual men in Africa, but it is unclear if circumcision may reduce HIV acquisition among men who have sex with men (MSM) in the United States, or whether MSM would be willing to be circumcised if recommended. Methods We interviewed presumed-HIV negative MSM at gay pride events in 2006. We asked uncircumcised respondents about willingness to be circumcised if it were proven to reduce risk of HIV among MSM and perceived barriers to circumcision. Multivariate logistic regression was used to identify covariates associated with willingness to be circumcised. Results Of 780 MSM, 133 (17%) were uncircumcised. Of these, 71 (53%) were willing to be circumcised. Willingness was associated with black race (exact odds ratio [OR]: 3.4, 95% confidence interval [CI]: 1.3–9.8), non-injection drug use (OR: 6.1, 95% CI: 1.8–23.7) and perceived reduced risk of penile cancer (OR: 4.7, 95% CI: 2.0–11.9). The most commonly endorsed concerns about circumcision were post-surgical pain and wound infection. Conclusions Over half of uncircumcised MSM, especially black MSM, expressed willingness to be circumcised. Perceived risks and benefits of circumcision should be a part of educational materials if circumcision is recommended for MSM

in the United States.

EDITOR'S NOTE: The full text of this article is available for public access at the above website.

August 2008 Supplement of AIDS Journal focuses on social justice and human rights

<http://www.aidsonline.com/pt/re/aids/toc.00002030-200808002-00000.htm;jsessionid=LFZLrRS9t3KG04QqTgTrTQ8XVnTMJdg2whhlMnqqP4QHK4c8pRd5!1629792715!181195629!8091!-1>

This Supplement to Volume 22 of AIDS Journal will focus on social justice and human rights. The full table of contents is available at the above website.

August 2008 Supplement of STI Journal: Improved data, methods and tools for the 2007 HIV and AIDS estimates and projections

http://sti.bmj.com/content/vol84/Suppl_1/?etoc

This Supplement to Volume 84 of STI Journal provides articles aimed at "Improved data, methods and tools for the 2007 HIV and AIDS estimates and projections." The full table of contents is available at the above website.

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6. EPIDEMIOLOGY

"AIDS among Latinos on rise"

Date: 23 July 2008

Source: *The Washington Post*

Author(s): Ceci Connolly

<http://www.washingtonpost.com/wp-dyn/content/article/2008/07/22/AR2008072202837.html?hpid=artslot>

AIDS rates in the nation's Latino community are increasing and, with little notice, have reached what experts are calling a simmering public health crisis.

Though Hispanics make up about 14 percent of the U.S. population, they represented 22 percent of new HIV and AIDS diagnoses tallied by federal officials in 2006. According to a survey by the Kaiser Family Foundation, Hispanics in the District have the highest rate of new AIDS cases in the country.

So far, the toll of AIDS in the nation's largest and fastest-growing minority population has mostly been overshadowed by the epidemic among African Americans and gay white men. Yet in major U.S. cities, as many as 1 in 4 gay Hispanic men has HIV, a rate on par with sub-Saharan Africa.

Blacks still have the highest HIV rates in the country, but language difficulties, cultural barriers and, in many cases, issues of legal status make the threat in the Hispanic community unique. For those who arrived illegally, in particular, fear of arrest and deportation presents a daunting obstacle to seeking diagnosis and treatment.

"Officials need to stop downplaying or ignoring what's happening among Latinos," said Oscar De La O, president of Bienestar, a Latino service organization. "We are at the center of the storm."

Even with the United States embroiled in a fierce debate over immigration policy, the problem of AIDS in Latinos had received scant attention from political and public health officials. At the Centers for Disease Control and Prevention, where only two of 17 approved HIV programs target Hispanic Americans, officials have added Spanish-language hotlines, confidential testing sites and other initiatives aimed at filling the gap.

"Hispanics are overrepresented in this epidemic, and we need to target our efforts to them," CDC epidemiologist Kenneth Dominguez said in an interview.

Officials do not have a precise tally of HIV infection nationwide, because many states have not reported figures to the CDC. The 22 percent, a figure that has not been previously released, includes 33 states and Puerto Rico, but not California, where more than 37 percent of the population is Hispanic.

"You combine the economic pressures, loneliness and immigration worries, and it pushes these individuals to be a hidden population," said Frank Galvan of the Charles Drew University of Medicine and Science in Los Angeles.

The consequences, however, go well beyond the Hispanic community. If the United States does not begin to "make a dent" in the swelling crisis of HIV among Hispanics, Galvan said, "it will continue to spread to other populations."

The nexus of AIDS and migration -- the reality that viruses know no borders -- will gain fresh prominence at the International AIDS Conference next month in Mexico City. It is a nexus that plays out in dramatic fashion in San Ysidro and other communities along the U.S.-Mexican border, where the tensions associated with immigration tend to exacerbate an already stigmatized illness.

"Migrants tend to be lonely, separated from their family or partners," Dominguez said. "They do not have health insurance. They may turn to drugs or alcohol. All of these put a migrant at higher risk."

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EDITOR'S NOTE: *The full text of this article is available for public access at the above website.*

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7. HIV/AIDS VACCINES

"Trial for vaccine against H.I.V. is canceled"

Date: 18 July 2008

Source: *The New York Times*

Author(s): Lawrence K Altman

http://www.nytimes.com/2008/07/18/health/18vaccine.html?_r=1&oref=slogin

Plans for a large human trial of a promising government-developed H.I.V. vaccine in the United States were canceled Thursday because a top federal official said scientists realized that they did not know enough about how H.I.V. vaccines and the immune system interact.

The decision is a major setback in an effort to develop an H.I.V. vaccine that began 24 years ago when government health officials promised a marketed vaccine by 1987. Health officials have long contended that such a vaccine would be their best weapon to control the AIDS pandemic.

A number of other H.I.V. vaccines are in various stages of testing around the world. But there had been high hopes for the government's trial because the potential vaccine was among a new class that sought to stimulate the immune

system in a different way.

The official who canceled the government trial, Dr. Anthony S. Fauci, director of the National Institute of Allergy and Infectious Diseases, said it was becoming clearer that more fundamental research and animal testing would be needed before an H.I.V. vaccine was ever marketed.

Scientists say that developing a vaccine against H.I.V. is one of the most difficult scientific endeavors in history because of the uncanny nature of the virus.

The government vaccine — known as PAVE, for Partnership for AIDS Vaccine Evaluation — was similar to a much-heralded vaccine that failed last year. That vaccine was developed by Merck, and Dr. Fauci's agency helped pay for the Merck trials.

Dr. Fauci said he reached his decision to cancel the coming trial after meeting with scientists to try to understand why the Merck vaccine had failed. He said he had concluded that scientists must go a step at a time because they did not yet know fundamental facts like which immune reactions are the most important in preventing the infection.

Dr. Fauci said the new trial was intended to determine whether the vaccine could significantly lower the amount of H.I.V. in the blood of those who become infected. He said a smaller trial was needed to figure out whether the vaccine could do that before large trials were conducted.

“Show me that the vaccine works by lowering the amount of H.I.V. in the blood,” Dr. Fauci said. “Then we will move to a larger trial that will document the link with a particular immune response.” He added that until then, “doing a large trial is not justified.”

Dr. Alan Bernstein, executive director of the Global HIV Vaccine Enterprise, said that his organization supported Dr. Fauci's decision and that there was an “urgent need for a diversity of new approaches to H.I.V. vaccine design.” For instance, Dr. Bernstein said, recent laboratory advances, which allow scientists to look at hundreds of genes simultaneously, “offer immense promise in helping us understand how to design new H.I.V. vaccine candidates that can achieve long-lasting immune protection.”

The trial canceled Thursday was supposed to have started enrolling 8,500 volunteers last October to receive the PAVE vaccine, developed by the infectious diseases agency. PAVE is a consortium of federal agencies and key federally financed organizations involved in developing and evaluating experimental H.I.V. vaccines. It seeks to create an effective H.I.V. vaccine that no pharmaceutical company or institution is likely to accomplish on its own.

The PAVE trial had been postponed after a test of the Merck vaccine failed in its two main objectives: to prevent infection and to lower the amount of H.I.V. in the blood among those who became infected. Also, the findings among the 3,000 participants in nine countries in which the Merck vaccine was tested suggested it might have increased the risk of becoming infected.

After a safety monitoring committee detected the problems with the Merck vaccine in September, the company quickly halted its study.

Scientists have found no obvious explanation for the failure of the Merck vaccine, which had been considered the most promising candidate.

The Merck vaccine was the first of a new class of H.I.V. vaccines to get to an advanced stage in human testing. The vaccine was made from a weakened version of a common cold virus, adenovirus type 5, which served as a way to deliver three synthetically produced genes — gag, pol and nef — from the AIDS virus. Three doses of the vaccine were injected over six months.

Scientific analyses found that the highest risk of H.I.V. infection among recipients of the Merck vaccine was in males who both were uncircumcised and had pre-existing antibodies to adenovirus type 5.

After the failure of Merck trial, the government reduced the number of potential volunteers to 2,400; they would have included circumcised gay men who had no pre-existing antibodies to adenovirus type 5. The scaled-back study would have cost about \$63 million, compared with \$140 million for the initial design.

At a news conference in 1984, top federal officials said they were optimistic that a marketable H.I.V. vaccine would be available in three years. Since then, AIDS researchers have been divided about how fast to test experimental vaccines.

Many urge caution out of fear that failures could destroy confidence among uninfected people most at risk who would be needed as volunteers in future trials.

But equally vocal groups call for testing everything as soon as the research shows promise because of the urgent need for a vaccine.

In an unrelated development, researchers at Duke University reported new findings Thursday showing that H.I.V. stuns the immune system earlier than scientists previously understood.

The window of opportunity in stopping H.I.V. may be a matter concerning the first few days, not weeks, after the virus enters the body, a team headed by Dr. Barton Haynes reported in *The Journal of Virology*.

The findings were based on a study of 30 individuals newly infected with H.I.V., and the National Institutes of Health paid for the study.

EDITOR'S NOTE: AIDS Vaccine Advocacy Coalition (AVAC) issued a statement on NIAID's decision, available here: http://www.avac.org/pdf/AVAC_statement_PAVE100.July17.pdf.

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8. OTHER PREVENTION APPROACHES

"MSM Prep study to kick off in Cape Town"

Date: 22 July 2008

Source: *Health-e*

<http://www.health-e.org.za/news/article.php?uid=20032027>

Prep is a therapy taken to prevent, rather than to treat, an infection or illness, and it is one strategy being studied by the University of Cape Town's Desmond Tutu HIV Foundation, as part of its effort to develop new HIV prevention tools.

This study is designed to determine whether a once daily oral dose of the HIV antiretroviral drug Truvada (tenofovir disoproxil fumarate and emtricitabine) will provide additional protection against HIV infection when combined with risk reduction and condom use counseling.

The study will enroll 200 healthy, sexually active, HIV-negative men who have sex with men (MSM) who are at high risk of HIV infection. Potential volunteers will be extensively interviewed to ensure that they understand the study and that their participation is completely voluntary. Consenting study participants will be carefully monitored throughout the 24-month study period and for 6 months afterwards. All study participants will receive condoms and counseling on how to prevent HIV infection, and medical care for any sexually transmitted infections on a monthly basis.

Approximately half will also receive the study drug Truvada once daily, and half will receive a placebo. Neither the study personnel nor the volunteers will know who is receiving the drug and who is receiving

placebo. In addition to extensive safer sex counseling, volunteers will be counseled that, even if they receive the study drug, there is no assurance that the drug will offer any protection against HIV infection and that safer sex precautions should always be used.

Truvada was selected for the Cape Town Prep study because it has been shown to be a safe and effective treatment for HIV, with few side effects in studies involving more than 15 000 people worldwide. The tenofovir plus emtricitabine drug combination of Truvada was approved for use by the Food and Drug Administration in the United States in 2004, and in South Africa by the Medicine Control Council in 2007. More than 100 000 HIV-infected people around the world have now used these drugs.

The National Institutes of Health and the Bill and Melinda Gate Foundation are sponsoring the Cape Town Prep study through a grant to the J. David Gladstone Institutes, a non-profit independent research organization affiliated with the University of California, San Francisco.

The Desmond Tutu HIV Foundation is a registered non-profit organization that has developed a robust HIV prevention research agenda focusing on disenfranchised population - particularly young women and MSM.

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9. NON-HIV STIS AND REPRODUCTIVE HEALTH

Population Report: New Findings on Contraceptives

<http://www.infoforhealth.org/pr/m20/NewFindings.pdf>

Scores of health research findings appear every year. However, most of them do not get transferred into clinical practice because health care providers do not have the time to sort through all the information, or have limited access to it. The lag in research-to-practice for findings on contraceptive methods is addressed in the latest issue of Population Reports, “New Findings on Contraceptives,” from the Johns Hopkins Bloomberg School of Public Health. The report also summarizes new research findings on contraceptive methods, interprets these findings in the context of previous research, and suggests implications for practice.

New research findings highlighted in the 20-page report published by the INFO Project at the Johns Hopkins Center for Communication Programs include:

- Providers can now give clients the DMPA injection even if they are four weeks late without otherwise ruling out pregnancy. Based on new research and the existing body of evidence, the World Health Organization (WHO) Expert Working Group released this new guidance in April 2008 on re-injection schedules of the progestin-only injectable depot medroxyprogesterone acetate (DMPA).
- Contrary to popular belief, a recent systematic review by the Cochrane Collaboration has shown that giving emergency contraceptive pills in advance does not result in increased sexual risk-taking. The mechanism of action of the progestin-only emergency contraceptive pills involves preventing ovulation.
- Family Health International has developed a new checklist to help providers identify women who are at low risk for current sexually transmitted infections (STIs). These women could be medically eligible for IUD insertion. In resource-poor settings, this checklist and other similar tools and approaches are essential for improving access to IUDs. For women wanting to start a contraceptive method soon after childbirth, the IUD is a convenient, safe option that provides long-term contraception.

The Population Reports issue pays special attention to the contraceptive needs of women with HIV. “Hormonal contraceptive methods do not increase the risk of becoming infected with HIV. Also, new evidence confirms the low risk of pelvic infection among IUD users with HIV, supporting WHO guidance that many women with HIV-related conditions generally can start using an IUD,” says author Deepa Ramchandran. Co-author Ruwaida Salem adds, “If a mother with HIV infection decides to breastfeed her infant, her health care provider should encourage and support her to breastfeed exclusively. Exclusive breastfeeding for the first six months of a baby’s life poses less risk of mother-to-child transmission of HIV than giving the baby formula or solid foods in addition to breast milk. In addition, the mother avoids unintended pregnancy through the Lactational Amenorrhea Method (LAM) of family planning.”

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10. POLITICS AND POLICY

"Selective reporting in clinical trials: analysis of trial protocols accepted by The Lancet"

Author(s): Al-Marzouki S, Roberts I, Evans S, et al

Reference: Lancet. 19 July 2008;372(9634):201.

<http://www.thelancet.com/journals/lancet/article/PIIS0140673608610600/fulltext>

Published Abstract:

Selective reporting in clinical trials occurs when outcome data are collected but not reported, and when investigators do many analyses but report only the most favourable. It can distort the results of trials¹ and bias meta-analyses.² We studied trial protocols that had been peer reviewed and accepted for publication in The Lancet to examine whether selective reporting of outcomes and subgroup analyses was present.

As of June, 2007, 75 protocols had been accepted, summaries of which were published on The Lancet's website. Four were excluded because they pertained to non-randomised trials. Of the remaining 71, we obtained permission to use 64. After contacting investigators and database searching, we identified published reports for 37 trials (50 reports). We checked consistency between protocols and published reports and assessed the prevalence of selective reporting of outcomes and subgroup analyses in the trial reports.

In 11 of the 37 trials, there were major differences between the protocols and the reports for primary outcomes. We found 64 primary outcomes in the protocols—a median of one per trial. However, in the published reports, there were 73 primary outcomes—a median of two per trial. Five trials had an unreported primary outcome and eight introduced a new primary outcome. In two trials the protocol primary outcome was reported as secondary. None of these trials published reasons for including or omitting outcomes or changing their status.

In these 37 trials, we found 158 secondary outcomes in the protocols—a median of four per trial. In the published reports, we found 123 secondary outcomes—a median of three per trial. 32 trials had at least one unreported secondary outcome or at least one new secondary outcome. Only 18 trials mentioned subgroup analysis in the protocols, but 28 reported it. Only one protocol gave the reason for subgroup selection. None specified the total number of subgroups. Among the 19 trials with no prespecified subgroup analyses in the protocol, subgroup analyses were done in 11. None gave the reason for these analyses. In the 18 trials in which subgroup analyses were prespecified in the protocol, 11 had at least one unreported subgroup analysis or at least one new subgroup analysis. Publication of protocols allows a comparison of what was planned with what was actually done, and this comparison should be possible during and after peer review.^{3,4} However, currently full protocols are not in the public domain and

authors' consent is needed for access.

Relatively little empirical research has been done on the quality of protocols, which can be deficient themselves. Web-based submission of protocols of clinical trials has been suggested.⁵ A mechanism, required by journals, for posting structured protocols in a standard format on the web might also improve the reliability and consistency of reporting. Online submission would oblige investigators to provide a complete protocol with all relevant fields completed. When the trial report was submitted, comparison between the protocol and the report would be easier and in future might be automated.

Although the solution to the problem of selective reporting requires further discussion, the current system is clearly inadequate.

EDITOR'S NOTE: *This article is available at its original location with a free subscription at the above website.*

"FDA moves forward with exempting Phase I drugs from GMPs"

Date: 16 July 2008

Source: *FDA News*

<http://www.fdanews.com/newsletter/article?articleId=108583&issueId=11771>

More than two years after withdrawing a final rule that would have exempted investigational drugs in Phase I testing from certain good manufacturing practice (GMP) regulations, the FDA is issuing a final rule to do just that.

The new rule, which amends the GMP regulation with the exact same language as the withdrawn rule, was published in Tuesday's Federal Register. Slated to take effect Sept. 15, it will apply to small-molecule drugs and biologics, including vaccines and gene therapy products.

"FDA's position is that the United States' [GMP] regulations were written primarily to address commercial manufacturing and do not consider the differences between early clinical supply manufacture and commercial manufacture," the agency says.

For example, the requirements for a fully validated manufacturing process, rotation of stock for drug product containers, repackaging and relabeling of drugs and separate packaging and production areas need not apply to investigational drug products made for use in Phase I trials, the agency says. In connection with the final rule on Phase I drug GMPs, the FDA issued a guidance recommending approaches to satisfy statutory GMP requirements for such drugs.

"During product development, the quality and safety of Phase I investigational drugs are maintained, in part, by having appropriate [quality control (QC)] procedures in effect," the guidance states. "Using established or standardized QC procedures and following appropriate cGMP will also facilitate the manufacture of equivalent or comparable IND product for future clinical trials as needed."

More information on the final rule can be accessed at www.fda.gov/OHRMS/DOCKETS/98fr/oc07114.pdf. A copy of the guidance, "CGMP for Phase 1 Investigational Drugs," can be viewed at www.fda.gov/OHRMS/DOCKETS/98fr/FDA-2005-D-0157-gdl.pdf.

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11. HIV/AIDS FUNDING

"Clinical trialists less likely to seek grant renewals"

Author(s):

Reference: Nature. 23 July 2008;454:381. News in Brief.

<http://www.nature.com/news/2008/080723/full/454381c.html>

Published Abstract: Clinical grant proposals receive poorer scores than their basic science counterparts from reviewers at the US National Institutes of Health (NIH), partly because clinical trialists are less likely to seek grant renewals.

A study published this month (M. R. Martin et al. *Am. J. Med.* 121, 637–641; 2008) examines review outcomes of almost 63,000 basic-science grant applications and more than 30,000 clinical grant applications reviewed between 2000 and 2004. It found that clinical applications were scored less favourably, which agrees with previous research.

About half of the difference was due to the failure, by some 15% of clinical proposals, to adequately address human-subject protection, the researchers say. The remainder was due to fewer clinical trialists (20%) competing to have their grant applications renewed compared with their basic science colleagues (28%).

This made a difference because the overall success rate of grant applications climbed with resubmissions: by the second round of resubmissions, differences between clinical and non-clinical application success rates had evaporated.

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12. ANNOUNCEMENTS

"New report calls for greater condom and contraceptive funding"

Date: 22 July 2008

Source: *Voice of America News*

Author(s): Joe De Capua

<http://voanews.com/english/Africa/2008-07-22-voa35.cfm>

A new report says more than 25 years into the AIDS epidemic, prevention remains a top priority in battling the disease. However, it says donor support for condoms and contraceptives in developing countries remains stagnant and far below projected needs.

The report, from Population Action International, will be formally presented early next month at the 17th International AIDS Conference in Mexico City. Some of the highlights were released Tuesday.

Amy Coen, president and CEO of Population Action International (PAI), says, "We really have to start looking at the future of the world and people's lives around this disease. And that means we have to work on making sure that it's not spread any further. Prevention has got to be integrated into policies and funding and programs at all levels of people's lives. We have to do all we can to stop the spread of HIV/AIDS."

Coen says abstinence is against human nature and therefore not a reliable prevention method. "Sexual activity is a strong human drive. It's a very good part, a happy part, hopefully, of all marriages and most

relationships. Asking people to stop having sex may sound good but has never worked any time in history. And it isn't working now," she says.

Coen says prevention must include both condoms and contraceptives, which can prevent unwanted pregnancies and mother-to-child transmission of the AIDS virus.

"We really, really have to scale up and integrate condoms and contraceptives into HIV prevention. I don't think people realize that contraceptives are indeed a prevention strategy and they are.... They have to be available. You can't walk two days to a clinic with a baby on your back and find out there are no contraceptives in the clinic," she says.

Also speaking at a news conference Tuesday was the report's co-author, Dr. Karen Hardee, who says in recent years the use of condoms has been deemphasized in favor of abstinence. She says, "An assessment was done a few years ago that showed that fewer than half of the people who wanted to use a condom during a sex act could obtain one. That's inexcusable 20 years into the HIV epidemic. And despite the fact that there are 2.5 million new HIV infections that occur every year, overall donor support in developing countries for condoms has remained largely unchanged over the past few years. Of the estimated 18 billion condoms that were needed in 2006, for example, donors provided just 2.3 billion. So not even half, not even a quarter," she says.

The report criticized the US PEPFAR program started by President Bush, saying it emphasized abstinence over condoms. PEPFAR officials have denied this, saying condoms have been a major part of the program. But they also say abstinence and being faithful did not receive enough attention.

EDITOR'S NOTE: The above-mentioned report by Population Action International is available for public access at

http://www.populationaction.org/Publications/Reports/Comprehensive_Hiv_Prevention/CompHIVPrevention.pdf

Clinical Scientist Awards in Translational Research

http://www.bwfund.org/programs/translational/clinical_scientists_main.html

Program Background

Basic research into the mechanisms of disease has accelerated in recent years, but the knowledge gained has been slow to reach the clinic and patient care. Both the translation of basic research knowledge into improved patient care and the translation of clinical insights into hypotheses that can be validated in the laboratory are threatened by changes in medical research and health care financing. The rapid growth of managed care, for example, has limited the financial resources available to many academic medical centers, which historically have been at the forefront of both basic and clinical research. Consequently, many physician-scientists, who play a critical role in identifying clinical questions and implementing advances in the basic sciences, have fewer financial resources, less time, and smaller patient populations available for clinical studies.

Recognizing this problem, the Clinical Scientist Awards in Translational Research program supports established independent physician-scientists who are dedicated to translational research—the two-way transfer between work at the laboratory bench and patient care. The program is intended to help protect award recipients' time to pursue the vital link between basic and clinical research. Importantly, the program

aims to identify and reward proven mentors and to increase their capacity to train the next generation of investigators skilled in translational research. In this way, BWF hopes to increase the ranks of experienced physician-scientists critically positioned to bridge the gap between bench and bedside.

EDITOR'S NOTE: Further information about these Awards is available at the above website.

Confronting the 'Evidence' in Evidence-Based HIV Prevention

<http://www.sfaf.org/files/site1/asset/sfaf-hiv-evidence-report-may-2008.pdf>

The report, “Confronting the ‘Evidence’ in Evidence-Based HIV Prevention,” summarizes many panel sessions hosted over the past year by SFAF, in partnership with the Caucus for Evidence-Based Prevention and other organizations. The Alliance co-organized one such panel with SFAF at the *Microbicides 2008* conference in Delhi, India. SFAF will distribute copies of this report at the Satellite Session in Mexico City, to be held Tuesday, August 5, 6:30 pm to 8:30 pm.

In Your Own Backyard: How NIH Funding Helps Your State's Economy

<http://www.familiesusa.org/issues/global-health/publications/in-your-own-backyard.html>

The National Institutes of Health (NIH) is America’s leading medical research agency and the foremost biomedical research institute in the world. The research funded by NIH has led to many dramatic improvements in our nation’s health, from decreases in deaths due to cancer, heart disease, and stroke to dramatic increases in life expectancy for patients with diabetes and HIV/AIDS.

Today, the continued preeminence of NIH—and even our position as the leader in biomedical research—is threatened because NIH is not adequately funded. For the past five years, federal funding for NIH has not kept pace with inflation: Since 2003, its purchasing power has actually declined by 13 percent.

Funding declines of that magnitude limit opportunities to make scientific advances that would improve our health here at home and advance the health of people worldwide. Promising research projects must be cut short, and a generation of scientists may opt to pursue other careers or may move to countries that are prioritizing the development of life sciences research.

But NIH funding cuts do more than stifle scientific progress—these cuts have a negative economic impact on communities across the country. Most Americans don’t know that NIH is a positive economic force in numerous local communities: Most of its \$29 billion budget—between 80 and 90 percent—funds research that takes place at universities, medical research centers, hospitals, and research institutes in every state in the U.S.

The federal dollars that NIH sends out into communities, known as “extramural funding,” provide real, direct economic benefits at the local level, including increased employment; growth opportunities for universities, medical centers, and local companies; and additional economic stimulus for the community. And when NIH funding is cut, communities across the country suffer too.

EDITOR'S NOTE: The above-mentioned report by Families USA is available for public access at

<http://www.familiesusa.org/assets/pdfs/global-health/in-your-own-backyard.pdf>

Microbicide Field Job Postings Now Available on AMD Website

http://www.microbicide.org/cs/employment_opportunities

Job availabilities in the microbicide field are now posted on the Alliance website.

- Medical Officer, CONRAD (Arlington, VA)
- Regulatory Administrator, Population Council (New York, NY)
- Statistician, Population Council (New York, NY)

New Resources from the International Women's Health Coalition (IWHC)

<http://www.iwhc.org/>

The International Women's Health Coalition (IWHC) is pleased to announce the following publications:

- Triple Jeopardy: Female Adolescence, Sexual Violence, and HIV/AIDS addresses the particular vulnerability of young women to sexual violence and HIV infection (<http://iwhc.org/resources/youngadolescents/triple-jeopardy.cfm>). This factsheet is the latest in the IWHC's series on Young Adolescents' Sexual and Reproductive Health and Rights (<http://iwhc.org/resources/youngadolescents>), which uses evidence about the sexual and reproductive knowledge and behaviors of 10- to 14-year-olds around the world to argue for more responsive programs and policies.
- Child Marriage: Girls 14 and Younger at Risk, underscores the realities of girls married at 14 or younger, including social and educational disadvantages, an elevated risk of contracting sexually transmitted infections including HIV, and complications in pregnancy and childbirth (<http://iwhc.org/resources/youngadolescents/childmarriage.cfm>; available in English, Spanish, Portuguese, and French).
- An updated version of Women and Risk of HIV/AIDS Infection, a factsheet highlighting the vulnerability of girls and women to HIV/AIDS (<http://iwhc.org/resources/hivaidsfactsheet.cfm>).

Please email wwelshimer@iwhc.org to request hard copies of the publications.

Value Added: Women and U.S. Foreign Aid Reform

<http://www.icrw.org/html/news/news.htm>

ICRW and Women Thrive Worldwide released today its think-piece on the issue of foreign aid reform in response to a broader reform agenda recently issued by the Modernizing Foreign Assistance Network (M-FAN), a group of U.S. think-tanks, academics and international nongovernmental organizations. The white paper, "Value Added: Women and U.S. Foreign Assistance for the 21st Century," emphasizes that investment in women is a crucial component of international development and should be a cornerstone of U.S. foreign assistance.

More than four decades of development experience shows that where gender inequalities persist, countries pay the high cost of slower economic growth, weaker governance and overall lower standards of living.

Without the integration of women, the ambitious goals of foreign aid reform will be met with only limited success.

To maximize the impact of U.S. foreign aid, the joint ICRW-Women Thrive Worldwide report recommends capitalizing on women's roles in reducing poverty and expanding economic growth, guaranteeing gender-equitable development assistance, and increasing funding and improving monitoring for programs that invest in women and address gender inequality.

Several recent Congressional hearings have focused on the state of U.S. foreign assistance, observing that its approach is based on the 1961 Foreign Assistance Act, which was framed to address obsolete security concerns pertaining to the Cold War. Rep. Berman, the Chair of the Foreign Affairs Committee in the House, has said that he wants to rewrite and modernize the above-mentioned Act. Potentially, this could mean the most serious overhaul in U.S. foreign aid policy since its conception.

EDITOR'S NOTE: The White Paper mentioned above is available at http://www.icrw.org/docs/ForeignAidReform_Gender08.pdf

What came out of G8?

The Center for Strategic and International Studies (CSIS) and the Henry J. Kaiser Family Foundation cordially invite you to attend a discussion of the 2008 G-8 Summit, held from July 7-9 in Hokkaido, Japan. It will cover outcomes related to climate change, global health, fulfillments of donor aid pledges to Africa, the global food crisis, and Zimbabwe.

When: Friday, July 25, 2008, 10a.m. ET - 12 noon ET

Where: CSIS, 1800 K Street, Washington D.C., 20006 NW, B1 Conference Center

Speakers:

- Professor Keizo Takemi: Research Fellow, Harvard School of Public Health Senior Fellow at the Japan Center for International Exchange (JCIE)
- Michael J. Green: Senior Advisor and Japan Chair, CSIS
- J. Stephen Morrison: Executive Director, HIV/AIDS Task Force, Director, Africa Program, CSIS
- Jennifer Kates: Vice President and Director of HIV Policy, Kaiser Family Foundation
- Daniel Sullivan (invited): Assistant Secretary, Bureau of Economic, Energy and Business Affairs, U.S. Department of State

Please RSVP to Heather Teixeira at Hteixeira@csis.org or at (202) 775-3213.

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