



ALLIANCE FOR MICROBICIDE DEVELOPMENT

13 July 2007, Volume 8, Number 27

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 complete issues of the Digest or search by keyword for individual articles at <http://www.microbicide.org/publications/>. 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. MEDIA COVERAGE OF MICROBICIDES

"Empowering women key step in fight against AIDS"

Date: 07 July 2007

Source: *The Nation*

Author(s): Elizabeth Mataka, Zeda Rosenberg

http://www.nationmedia.com/dailynation/nmgcontententry.asp?category_id=25&newsid=101795

More than 1,000 leaders from around the world came together in Nairobi this week to discuss issues related to HIV and Aids. While conferences on the pandemic are rather commonplace, this meeting was different. This time, African women - doctors, activists, nurses, grandmothers, community leaders, and women living with HIV - took centre stage at the International Women's Health Summit. It makes good sense that women are leading the fight against Aids. Some 60 per cent of Africans living with HIV are women. Among young people the situation is worse: More than 75 per cent of 15-24-year-olds living with HIV in Africa are women. In Kenya, young women are five times as likely as young men to be HIV positive. In Zambia, AIDS has reduced a woman's average life expectancy to 37 years. Across the continent, women are struggling to educate orphans, care for the sick, and feed their families under the weight of this epidemic.

Encouraging people to always use condoms and be faithful to one partner is important, but it is not enough. In fact, we know that in some cases marriage, or what a woman believes is a monogamous relationship, can actually increase a woman's risk of HIV. A woman may not be able to convince her partner to use condoms - or she and her partner may want to have children, which they cannot do while abstaining or using condoms. And remaining faithful to her husband cannot protect a woman whose husband is not faithful to her. To successfully defeat Aids we must do more to help women to protect themselves. A vaccine to prevent HIV, once developed, could save millions of lives. Another promising tool is a **microbicide**, a **vaginal gel**, ring or tablet that women could use to prevent infection.

Advocates in Africa

Microbicides are not yet available, but researchers and advocates in Africa and around the world are working to develop them and carry out clinical trials to test if they are safe and effective in preventing HIV infection. By putting protection from HIV into the hands of women, a **microbicide** would slow the spread of the virus and finally allow women to take control over their own health. We must prioritise research on these promising preventive technologies. At the same time, we must do more with the tools that already exist. The female condom should be affordable and accessible to women in Africa. We must expand prevention of mother-to-child-transmission services so that every pregnant woman receives the care and treatment she needs.

Like nearly all of us, the women attending this week's summit have lost family members, workmates, and friends to this disease. These women are on the frontlines every day - the doctor working long hours in the clinic, the grandmother who cares for her orphaned grandchildren, the community care worker visiting the homes of the sick, the woman living with HIV who had the courage to say so publicly, the sex worker who spends her days educating her peers at the taxi rank. These women are the ones who have told us of the desperate need for female-initiated HIV prevention approaches. After all, their lives and the future of our families and countries depend on it.

"Female condom use defended"

Date: 06 July 2007

Source: *The Nation*

Author(s): Caroline Wafula

<http://allafrica.com/stories/200707051412.html>

Delegates at an international meeting have dismissed claims that women do not like the female condom. Criticism of the condom tended to be based on the fact that few women in African countries had access to it and not many had been educated on its use, said the delegates at the World Young Women Christian Association (YWCA) meeting in Nairobi.

The executive director of the Joint United Nations Programme on HIV and Aids (UNAids), Dr Peter Piot, called on donors and governments to increase investment in female-initiated methods of HIV and Aids prevention, citing the female condom and **microbicides** as some of those that needed priority. The female condom must be fully funded and research on **microbicides** boosted, Dr Piot said at the official opening of the YWCA International Women's Summit yesterday. "We need to do better in terms of action that is relevant for women," he said.

Statistics indicate that only one female condom was available for every 100 women of reproductive age in Africa, Asia and Latin America last year. Reproductive health experts said research showed that women would demand the condom as an HIV prevention product if they had access to it and were shown how to use it. Women raised concern on whether it was safe to use the female condom more than once, due to its high cost. It also emerged that the device may only be accessed by the high and middle class, mostly in urban areas, shutting out those in rural areas and slums. Organisations such as the World Health Organisation (WHO), the United Nations Population Fund (UNFPA), Population Services International and Family Health International work closely with governments to provide the female condom in various countries at a reduced cost.

Reducing costs

Women who took part in the discussions at Kenyatta International Conference Centre (KICC) said increased financial investment in female condoms by donors and governments would greatly bring down the cost to affordable levels. An official of the Female Health Company in London, which manufactures the condom, said the firm expected to ship 25 million condoms to various countries this year, up from 20 million last year. Mr Robbie Nelson said the number of female condoms the company manufactured yearly had risen by between 20 and 40 per cent in the past four years. He said the number was small, compared to six billion male condoms distributed every year.

Loose morals

UNAids senior women and Aids advocacy officer Pauline Muchina said a positive image of the female condom was key to promoting its acceptability. "Many women still don't know about the condom because there has not been enough awareness on it," she said. The issue of stigma also arose, with women saying they feared buying or carrying condoms. Many shy away from asking for it for fear of being branded prostitutes or of loose morals, according to observations raised by delegates.

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2. PUBLISHED RESEARCH: MICROBICIDE-SPECIFIC

"A second chance for microbicides"

Author(s): Baleta A

Reference: N/A 370(9581):17-8. World Report.

<http://www.thelancet.com/journals/lancet/article/PIIS0140673607610290/fulltext>

Published Abstract: The launch in South Africa of the world's first trials of an antiretroviral-based **vaginal gel** is another chance for **microbicides** to prove their worth in HIV/AIDS prevention. But some experts are warning against placing too much hope on this method of protection. Women in the KwaZulu-Natal province of South Africa are signing up for the safety and efficacy trials of a **microbicide** gel, formulated with the antiretroviral tenofovir, which researchers hope will protect them from contracting HIV. If the gel works, it will be a major step forward in the quest for a female-controlled product to prevent infection. There are currently about 60 candidate **microbicides** being developed. Ten have proven safe and effective in animals and are now being tested in people in the USA, Africa, and

India. However, in the past year, three trials were stopped prematurely because the **microbicide** being tested was ineffective, and in some cases harmful.

Researchers at the Centre for the AIDS Programme of Research in South Africa (CAPRISA), which is leading the tenofovir trial, are undeterred. "I am excited and optimistic. We have a trial that potentially can make a difference in the epidemic", says CAPRISA director and co-principal investigator Salim Abdool Karim. "This is the first time that an antiretroviral is being used, and importantly, tenofovir has a superb safety profile and is highly efficacious in treating AIDS."

But Daniel Halperin, a senior research scientist at Harvard University School of Public Health warns that "although **microbicides** are clearly important, we also should not set too much store by the whole enterprise". He says that even if a successful **microbicide** is finally developed, it will "almost certainly" only provide part protection. "Unlike a vaccine or male circumcision, a **microbicide**, like a condom, will probably need to be applied before every sexual encounter, which typically happens spontaneously. Many people will probably not use a **microbicide** correctly and consistently", he adds. Halperin says **microbicides** could "undoubtedly" save some lives but adds that it is not clear what the actual population-level effect will be on the epidemic in a country like South Africa. "Other existing measures, not just hypothetical or hoped for interventions, such as promotion of partner reduction, promotion of condom use for high-risk groups like sex workers, and making safe male circumcision services more available have been shown to have an actual population-level impact."

President of the Medical Research Council in South Africa, Anthony Mbewu says mathematical modelling has shown that 2-5 million HIV infections could be averted over 3 years, if even 20% of women in contact with services in 73 lower-income countries used a 60% effective **microbicide**. "Averting HIV infection is not a light phrase. Infection is lethal for many women and saving a life is not a trivial matter."

Unlike other trials where women insert a dose of gel an hour before sex, women on the tenofovir trial can apply the gel 12 hours before sex and within 12 hours after sex. "This is especially useful for women who are partners of migrant workers and who do not have frequent sex", says Quarraisha Abdool Karim, who is co-principal investigator. She adds that women will be given free condoms and extensive counselling about risk reduction even though the gel can only be tested when it is used without a condom. "The reality however, is that many women are unable to either convince their partners to use condoms or to insist they be used all the time." Sex workers who have multiple partners, some of whom refuse condoms, will therefore be an important part of the trial. Beauty Mazibuko is recruiting sex workers and says it is a challenge to "work with them". "I sometimes have to go into the forest. It's not always easy to gain their trust and their time is money." She says, however, that they "are human beings" and some share information with their peers about the research and want to help.

According to the health department, KwaZulu-Natal's HIV prevalence rate of 39.1% tops the national average by 10%. About 1000 women will be enrolled for the tenofovir **microbicide** trial which has two sites, one in central Durban and the other in Vulindlela, a rural area 150 km away. "The nature of the epidemic in South Africa is unique. It is diffuse with similar levels of as high a risk among women in the general population as in sex workers", says Salim Abdool Karim. The HIV prevalence rate for women at the Durban eThekweni clinic is 59.3% and the rate for sex workers attending the clinic is 59.4%. At the rural Vulindlela research site, prevalence rates are also extremely high. About 55% of women aged 20-24 years old were HIV positive in 2004 compared with 44% in 2001.

In January this year the cancellation of the promising international phase III clinical trial to test the effectiveness of the cellulose sulphate (Ushercell) **microbicide**, was a major setback for millions of women and a great disappointment for researchers. The cellulose sulphate gel was not only ineffective but is thought to have increased the risk of infection in women who took part in the trial at the sites in India, Uganda, Benin, and South Africa. Commenting on the negative publicity in the aftermath of the Ushercell trial, Nomapondo Barnabus, who is involved in community participation in the tenofovir trial, says, "there was a lot of gossip about **microbicides**" but with the help of traditional healers, community leaders, and CAPRISA's community educators, people's concerns have been addressed. Gethwana Mahlase, in charge of recruiting rural women, says there were no health services in the Vulindlela before CAPRISA arrived in 2001. "They have provided a comprehensive service and are trusted by the community." She says people are "reassured because the antiretroviral [tenofovir] is already being used for treatment".

Mbewu says "as yet there is no hard evidence of what happened with the Ushercell trial. Trials must continue in the hope of finding a product to protect women". If proven effective, a **microbicide** could be a "remarkable intervention" in developing countries where men often refuse to wear condoms. It could also be beneficial in developed countries for high-risk groups that resist using condoms.

Salim Abdool Karim says the overall trend in **microbicides** has been to achieve greater specificity in action. The first-generation candidate **microbicides**, surfactants like nonoxynol-9, act broadly against sperm, sexually transmitted disease (STD), bacteria, and viruses. "The problem was that their broad action led to epithelial disruption which could increase the risk of HIV." The second-generation candidates, such as carrageenan, mostly have no effect on sperm or bacteria, and instead act against several viruses, including herpes simplex. The antiretroviral-based gels narrow the spectrum of action to HIV only. Importantly, although second-generation candidate **microbicides** (eg cellulose sulphate) block HIV from entering cells, the ARV-based gels are rapidly absorbed into the vaginal tissue and designed to inhibit viral replication within susceptible cells. "The flip side is that these antiretroviral-based gels do not have potential benefits like STD and pregnancy prevention", explains Salim Abdool Karim. Although there is "real disagreement" about preference of broad spectrum versus an HIV-specific approach he says it is "important to test different approaches and create diversity in the field".

Studies have shown that tenofovir has few side-effects and resistance is rare after short-term tenofovir monotherapy. Although it may occur after long-term exposure to the drug, it is infrequent. Only eight of 299 patients treated with a combination therapy develop resistance after 3 years. "It is important to note that tenofovir resistance is not life long, it is specific and does not confer resistance to a class of drugs", says Salim Abdool Karim.

Henry Gabelnick, executive director of CONRAD, a non-profit reproductive health organisation which is supplying the gel for the trial says: "The long half life of tenofovir will reduce the chance of non-compliance, increasing the chances of success."

Halperin warns that there is a danger - as with a potential vaccine or with male circumcision - of people migrating from using a more effective method, such as condoms or mutual fidelity, to a less effective one using a **microbicide** instead of a condom, or having multiple partners because of a false sense of security. "And because **microbicides** are not a one-time event, like circumcision, the cumulative risk of this migration could be even more substantial over time." However, he concedes that it is critical to develop more female-controlled methods, and to add as many weapons to the HIV/AIDS arsenal as possible.

"Biomedical HIV prevention-and social science"

Author(s): Imrie J, Elford J, Kippax S, et al

Reference: N/A 370(9581):10-11.

<http://www.thelancet.com/journals/lancet/article/PIIS0140673607610265/fulltext>

Published Abstract: The euphoria about biomedical interventions to prevent HIV that ignited the 2006 International AIDS Conference is about to be rekindled. The 2007 International AIDS Society (IAS) Conference on HIV Pathogenesis, Treatment and Prevention, in Sydney, Australia, has an entire track devoted to biomedical prevention. This conference will be important after what has already been an interesting year for prevention scientists.

During the past 12 months, two trials of male circumcision were stopped early because interim results showed such positive outcomes that it was considered unethical to continue. On the other hand, two trials of a **microbicide** compound were stopped early because of a suggestion of harm in one. Delegates attending IAS 2007 are certain to hear more about diaphragms, female condoms, **microbicides**, suppressive treatment of concurrent viral sexually transmitted infections, and pre-exposure and post exposure prophylaxis with antiretroviral therapy (ART), each of which will have varying degrees of efficacy. These developments are undoubtedly exciting and welcome, because for several years primary prevention of HIV has taken a backseat while delivery of HIV treatment has been in front. Successful trials will bring more calls for high-tech solutions. International policy and funding agencies will offer extra money for trials of new interventions, and for implementation and scale-up of others. But there is a case for considering carefully what should happen next.

It is important to remember that efficacy is not the same as effectiveness. All trials of biomedical interventions to prevent HIV have biological markers or reduced HIV transmission as the primary endpoint. Their aim is to show efficacy (health improvement under ideal circumstances, in expert hands), rather than effectiveness (impact on health, under real-world conditions, for entire populations). But the demonstration of efficacy can be problematic. Unexpected events, such as participants not using products as instructed and participants in the control group adopting other protective strategies, have undermined recent trials.

The effectiveness of biomedical prevention is something we still know little about. So far, no intervention has been rolled out such that the impact on health outcomes for entire populations can be estimated. Even large trials collect only limited data on social or cultural acceptability and intervention uptake beyond the trial setting. In most contexts, we barely know what is needed for scale-up or what support there is, or what behavioural consequences might accompany interventions. Education campaigns that explain interventions are nearly non-existent. The communication of concepts such as "partly effective" or "protection derived from combining interventions with condoms" needs social scientists working with communities to help grasp the nature of risk and protection. Before scaling-up, we need high-quality social and behavioural research that prepares the ground, highlights potential pitfalls, and flags unanticipated consequences. We also need the courage to learn from experience.

The consequences of ART as a prevention intervention at the population level in men who have sex with men illustrate why social and behavioural science research needs to precede scale-up. Theoretically, widespread uptake of

ART should reduce overall viral load in the HIV-infected population, thus limiting transmission with or without behavioural change. Yet international surveillance data show only isolated examples of the stabilisation of HIV incidence in men who have sex with men, when ART is widely available. One conclusion of a systematic review of research in men who have sex with men between 1996 and 2003 was that the likelihood of reporting unprotected sex was significantly higher in those who believed ART reduced HIV transmission or who were less concerned about HIV, in view of the availability of ART. The message is simple: we must take potential unintended consequences and disinhibition in the context of prevention interventions seriously.

Biomedical prevention interventions offer large promise, but are not a panacea. Efficacious interventions need to be embraced, incorporated into our repertoire, and scaled up quickly. But we owe it to those who might benefit from these interventions to do everything possible to maximise their effectiveness at a population level. We should begin by answering questions about individual versus social and cultural acceptability, scale-up requirements, feasibility, and delivery, and set up behaviour-monitoring mechanisms to gauge impact, changes over time, and intended and unintended outcomes. These are all daily chores for social and behavioural scientists. How to build better working relations between trialists and social scientists, how to undertake the social research that is needed to support any scale-up while trials are ongoing, and how to release the financial and capacity resources to do all that are all questions IAS conference delegates might want to consider on their journeys home from Sydney.

EDITOR'S NOTE: This article, complete with references, is available at the above website.

Entry Inhibitors as Microbicides - newly published book chapter

<http://www.springer.com/west/home/generic/search/results?SGWID=4-40109-22-173708527-0>

Entry Inhibitors in HIV Therapy presents the current status of this relatively new and highly dynamic class of inhibitors and provides a unique overview of obstacles and considerations for HIV entry inhibition compared to other antiretroviral targets.

The introductory chapters of this book present an overview of entry inhibitors, review current knowledge of how Env mediates entry, and discuss the challenge of genetic diversity in this region of the viral genome. Subsequent chapters feature current information on individual classes of entry inhibitors that target each step of the virus entry pathway, from attachment to membrane fusion. There is an emphasis on the complex determinants of entry inhibitor susceptibility, resistance mechanisms, the need for clinical phenotyping, and how these issues create new challenges for antiretroviral therapy. Encouraging pre-clinical studies of entry inhibitors as **microbicides** are also discussed. The final chapters highlight the current status of entry inhibitors in clinical studies, the major milestone achieved with FDA approval of enfuvirtide, and review drug development, past and present.

In summary, this book presents a comprehensive and current overview of entry inhibitors from an expert panel of authors with diverse backgrounds and perspectives, incorporating many unrelenting successes against a backdrop of formidable challenges. It is of interest to basic science researchers as well as clinical physicians.

Book: *Entry Inhibitors in HIV Therapy*, JD Reeves and CA Derdeyn (eds.), published by Birkhauser. Chapter: Entry Inhibitors as **Microbicides** by Clyde Hart and Tammy-Evans Strickfaden, Division of HIV/AIDS, Centers for Disease

Control and Prevention, Atlanta, GA 30333.

"Pre-exposure prophylaxis for HIV infection: what if it works?"

Author(s): Paxton LA, Hope T, Jaffe HW

Reference: N/A 370(9581):89-93.

http://w3.nexis.com/new/results/docview/attachRetrieve.do?csi=227500&A=0.12318525689805926&risb=21_T1750817220&urlEnc=ISO-8859-1&inline=y&smi=7335&componentseq=1&key=4407610538&type=pdf

Published Abstract: For all the advances in treatment of HIV infection, the mainstays of prevention have changed little: sexual abstinence, condoms, sterile injection equipment, avoidance of high-risk behaviours, and knowing one's own serostatus and that of any sexual or drug-injecting partners. Although these strategies can be effective and recent years have seen decreases in new infections in some countries and in some risk groups, the 11000 new infections daily is ample testament that additional methods of prevention are needed.

Evidence for successful HIV-prevention technologies is mixed. Randomised studies of male circumcision in South Africa, Kenya, and Uganda were discontinued early after interim review showed reductions in new HIV infections ranging from 60 to 74 in the circumcised men compared with those who were not circumcised. Several topical **microbicides** are in advanced trials. However, phase III trials of C-31G (originally developed by Cellegy Pharmaceuticals) and cellulose sulphate (Polydex Pharmaceuticals, Nassau, Bahamas) were terminated early because preliminary results suggested no efficacy (C-31G) or increased risk of HIV transmission (cellulose sulphate). HIV-vaccine research continues despite two completed trials of AidsVax (VaxGen, South San Francisco, CA, USA) that showed no efficacy. Proof of efficacy of any present **microbicide** or vaccine candidate is several years away, and first products will probably be only moderately effective. The need to manufacture such a product in large quantities and distribute it around the world will pose additional challenges.

Pre-exposure prophylaxis

Disease prevention by prophylactic drugs is standard practice in travellers to malaria-endemic countries and for other infections such as *Pneumocystis jirovecii* in HIV infection. Various studies show that antiretroviral treatment given at or shortly after an exposure can substantially reduce HIV transmission: prompt treatment clearly increases effectiveness. This observation led to the hypothesis that transmission could be decreased further if treatment was delivered before exposure to HIV. Several primate models of such pre-exposure prophylaxis have shown efficacy.

For years, pre-exposure prophylaxis was not thought feasible for human beings because no antiretroviral agents met criteria for long-term use by healthy people (eg, high potency against HIV, simple dosing schedule, low rates of adverse effects, and low frequency of drug-induced resistance). However, in 2001 such a drug was approved; the nucleotide reverse transcriptase inhibitor tenofovir. The combination treatment of tenofovir and another nucleoside reverse transcriptase inhibitor, emtricitabine, was approved in 2004.

A phase II safety study in 936 female sex workers in Ghana, Nigeria, and Cameroon showed no difference in the frequency of adverse events between those taking tenofovir and placebo. Two women seroconverted to HIV-positive status in the tenofovir group compared with six in the placebo group, but this difference was not significant. A phase II

study of 400 men who have sex with men is in progress in the USA, and three randomised, placebo-controlled efficacy trials of pre-exposure prophylaxis are underway or will start soon: use of tenofovir in injecting drug users in Thailand; tenofovir and emtricitabine in heterosexual men and women in Botswana; and tenofovir and emtricitabine in men who have sex with men in Peru and Ecuador. Preliminary results from these trials are expected from 2008. By contrast with new agents, such as HIV vaccines or **microbicides**, both tenofovir and emtricitabine are already widely available in many countries.

Availability of these drugs could be a double-edged sword if it leads to their misuse. Anecdotal reports are already circulating, of physicians prescribing tenofovir to patients at high risk of HIV infection, and of unregulated use of the drug at venues such as sex clubs and circuit parties. Even those who would provide pre-exposure prophylactic treatment, such as doctors and other health-care providers are unsure about appropriate indications. If present trials show efficacy of tenofovir (or tenofovir and emtricitabine) against HIV transmission, the pressure for immediate approval for prevention will be great. Thus, the public-health community needs to begin planning for such demands before the trials are completed.

Drug toxicity and viral resistance

Tenofovir (and tenofovir and emtricitabine) has a good safety profile and infrequent side-effects; the most common side-effects are gastrointestinal discomfort, dizziness, headache, and rash. Less than 1 of patients with HIV taking tenofovir in clinical trials had serious drug-related adverse events such as acute renal failure, Fanconi's syndrome resulting in severe hypophosphataemia, decreases in bone-mineral density, and rarely, lactic acidosis. Tenofovir plus emtricitabine has the same adverse effect profile as tenofovir, except for occasional skin hyperpigmentation. Such side-effects are usually reversible if treatment is stopped, but are serious nevertheless. Regular monitoring will be needed to detect such adverse effects and ones that might occur only in HIV-negative people.

Evolution of drug resistance is a worry if a prophylactic regimen is used by someone already infected with HIV. Because the use-effectiveness of pre-exposure prophylaxis cannot be 100, some people will become infected while taking it, thus some drug resistance might occur. Moreover, informal drug sharing, black-market use, or imperfect screening might result in some people who are HIV-positive inadvertently taking prophylaxis. One drug might be effective for prevention of infection, but a regimen of one or two drugs in established infection can be detrimental if viral resistance mutations develop, resulting in restricted future treatment options.

The classic pathway to tenofovir resistance in patients without previous drug treatment is the selection of one mutation, K65R. In studies of individuals with HIV taking combination antiretroviral therapy, this mutation was detected in 3-2 of people over 96 weeks of follow-up. Small phase I studies of tenofovir monotherapy in people with HIV did not show development of any drug resistance mutations with up to 28 days of treatment, but in macaques infected with simian immunodeficiency virus, ultrasensitive resistance tests showed rapid development of K65R in those with high viral loads given high doses of tenofovir. The K65R mutation also causes some resistance to other nucleoside reverse transcriptase inhibitors and increased susceptibility to zidovudine.

Emtricitabine induces the selection of its signature mutation, M184V, more frequently than tenofovir induces selection of K65R. M184V confers high resistance to emtricitabine and lamivudine. However, it causes lower cross-resistance to other nucleotide reverse transcriptase inhibitors than K65R, and it can partially reverse T215Y-mediated resistance to zidovudine, tenofovir, and stavudine. A combination of two drugs, (ie, tenofovir and emtricitabine) for HIV prevention might result in less risk of resistance than one agent, similar to the effect of combination therapy in HIV treatment.

Increased risky behaviours

Mathematical modelling of HIV transmission by people taking antiretroviral drugs suggests that reduction or reversal of any benefits could result from a small increase in risky sexual behaviour. Although pre-exposure prophylaxis might greatly reduce HIV transmission, this effect could diminish if people taking such prophylaxis increase their risky behaviour. Moreover, HIV prophylaxis offers no protection against other sexually transmitted infections.

Present trials should provide data for risky behaviours associated with pre-exposure prophylaxis. Previous trials of other interventions for reduction of HIV transmission are not directly comparable with pre-exposure prophylaxis, but suggest that increases in risky behaviour are less than feared. In the previously mentioned AidsVax, no increases in risky sexual or drug use behaviours were seen. Most studies of people taking post-exposure HIV prophylaxis show no increases in risky behaviour and a meta-analysis of several studies of people with HIV showed no differences in sexual behaviour between people with HIV taking antiretroviral therapy and those who were not. However, people who thought that drug treatment prevented transmission or those who were unconcerned about transmission because of the availability of antiretroviral treatment were more likely to report engaging in unprotected sex than those who did not express such beliefs. These observations highlight the importance of education and close monitoring of people taking pre-exposure prophylaxis to detect increased risky behaviour.

Ethics

The possibility of pre-exposure prophylaxis for HIV raises important ethical questions such as: what are the obligations of governments and industry to provide such prophylaxis? How should resources be distributed between research, treatment, counselling, testing, primary prevention, pre-exposure prophylaxis, and post-exposure prophylaxis? Who should have priority for prophylaxis? These types of issues arise in many health-care settings; however stigma associated with HIV poses particular challenges. General ethical principles for informing public-health policy should not be distorted because of such stigma. A problem with stigmatisation is that prejudices can affect decisionmaking without discussion and assessment of underlying beliefs. Perhaps the most important prejudices relate to risky behaviours.

One argument against provision of pre-exposure prophylaxis for groups such as sex workers, drug users, and men who have sex with men is based on the idea that providing prophylaxis expresses approval for high-risk behaviours. Analogous arguments include those against provision of clean needles for injecting drug users or condoms for teenagers. We reject this argument for several reasons. First, public-health policy should aim for prevention of ill-health rather than judgments of individual's morality. Second, we do not believe that provision of prophylaxis condones risky behaviour; but rather, it acknowledges the reality of the epidemic.

Another issue is the perception that people choosing risky behaviours should be at lower priority for prevention than those whose risk is not affected by their behaviour. The second category includes women infected by their spouses or infants infected by transmission from their mothers. In discussing African women with AIDS in 2003, UN Secretary General Kofi Annan noted "often they are the innocent victims". Although this term is appealing for the purpose of drawing attention to specific groups affected by HIV/AIDS, it has no place in public-health planning or priority setting. Even if personal responsibility for infection was considered in setting public-health priorities, how does one ascribe the degree of responsibility? Is a person who was brought up in an environment in which smoking was strongly encouraged responsible for the ill-health that results from their addiction? How would one judge the responsibility of female sex workers in developing countries in view of the social and economic pressures to which they are subjected? Generally, no method of ascribing personal responsibility for disease is reliable or valid. We therefore believe that

neither judgments about morality, nor responsibility for risky behaviours should play a part in decisionmaking about pre-exposure prophylaxis. Instead, public-health decisions should be based on relevant factors such as cost-effectiveness and clinical need.

Public-health issues

Mathematical models of pre-exposure prophylaxis³⁵ and topical anti-HIV **microbicides**, suggest that even a partially effective product could avert many infections. The trials of pre-exposure prophylaxis will provide important safety and efficacy data for prevention of HIV transmission by injecting drug users and through sexual intercourse. However, even after these trials conclude many information gaps will remain. Perhaps most important is that not all groups at risk are included. For example, adolescents and pregnant women in countries with high HIV prevalence are especially vulnerable, for both social and biological reasons, yet they are excluded from the trials. For adolescents, exclusion is mainly because of legal restrictions on the age of consent for trial participation. Pregnant women are usually excluded because of concerns about fetal exposure to antiretroviral drugs in the absence of proof of efficacy for prevention of HIV transmission to the mother.

The trials will also provide valuable information about drug toxicity, viral resistance, and increases in risky behaviours. However, few seroconversions are expected in participants taking tenofovir or tenofovir and emtricitabine, and participants have risk-reduction counselling and monitoring that would be difficult to reproduce outside the controlled environment of a study, thus trial results might not be entirely true to what would be seen in practice. All these factors will need to be considered in planning for implementation.

The main elements of a pre-exposure prophylaxis programme will be constant irrespective of the setting: every programme will need infrastructure for drug distribution; guidelines for use should be developed before implementation of the intervention; and HIV counselling and testing services need to be readily available. Individuals taking pre-exposure prophylaxis will need regular clinical monitoring for adverse drug effects, incident HIV infection, and increases in risky behaviour. People who become infected while taking the drug should have viral resistance testing and access to appropriate treatment regimens. Successful implementation of any pre-exposure prophylaxis programme will need plans for educating communities at risk about the drug's availability and its use, and to warn against increases in risky behaviour. All these parts of an implementation programme will need health workers to be trained, and probably the recruitment of additional staff.

Drug costs will be high. The average cost of 30 days supply of tenofovir in the USA is 523 and for tenofovir and emtricitabine it is 869. Gilead Sciences, the manufacturer of both drugs, has developed a programme for worldwide access and is working with WHO to make these drugs available for any approved use in 97 developing countries at no profit, presently around 17 a month for tenofovir and 26 a month for combination treatment. But even at these prices treatment will be too expensive for many people at greatest risk of HIV. The costs of getting the drug to people, and those of training health workers to prescribe and monitor the intervention will also be substantial.

By contrast with developing countries, most industrialised countries have high income per head, better health-care infrastructure, low HIV incidence, and HIV epidemics that disproportionately affect identifiable risk groups. For example, in the USA, nearly half of new infections occur in men who have sex with men. Education strategies, guidelines for use, and other elements of an intervention plan for this group would differ from those directed at women. Additionally, in industrialised countries, factors that might not be as important in developing countries, such as recreational drug use and so-called prevention fatigue (ie, people know about HIV and AIDS and risk reduction

strategies but become complacent about protecting themselves) affect HIV transmission and could in turn affect the success of a prophylaxis programme.

If pre-exposure prophylaxis is shown to be effective, this intervention should quickly be made available to populations at greatest risk of HIV. However, current HIV-prevention programmes are substantially underfunded and even proven and simple interventions, such as voluntary counselling and testing, access to condoms, programmes of education for behaviour change and for harm reduction in injecting drug users, do not reach the people who need them most. Estimates suggest fewer than one in five people at high risk in low and middle income countries have access to such proven prevention methods. New interventions against HIV, including pre-exposure prophylaxis, should always be regarded as a component of prevention and not a replacement for existing methods, and should be integrated as much as possible into existing programmes. Ideally, resource allocation to pre-exposure prophylaxis should not be at the expense of other programmes. In practice, competition for prevention resources will arise unless substantial new resources are allocated.

Steps to take today

In August, 2006, the Global HIV Prevention Working Group, an international panel of more than 50 experts on HIV and AIDS, was convened by the Bill and Melinda Gates Foundation to discuss HIV-prevention research, and released a report about factors necessary for enabling access to new HIV-prevention technology. These factors include early commitment of resources from donors, coordination between governments and regulatory agencies, and planning of guidelines for use. Although the first results from pre-exposure prophylaxis trials are expected around 2008, few of these recommendations are practised. However, since the efficacy of pre-exposure prophylaxis is not established, such a delay in planning is understandable. If trials of pre-exposure prophylaxis are successful, its use still might not be supported because many other HIV-prevention programmes are underfunded. Nevertheless, the severity of the HIV epidemic and the potential benefits of pre-exposure prophylaxis should lead us to begin planning for implementation as soon as possible. Public-health policymakers and implementers first need to decide which settings are appropriate for the intervention. What level of efficacy would warrant widespread use of pre-exposure prophylaxis? Which populations would benefit most from such a programme? In regions with HIV epidemics in specific groups, targeting of such groups (eg, sex workers, partners of people known to have HIV, and those attending sexual-health clinics) is probably the best strategy. However, in areas with generalised epidemics, as is seen in some African countries, potential populations could include most sexually active adults. Risks, benefits, and costs of different implementation strategies need to be considered carefully. Mathematical modelling could be very helpful for such difficult decisionmaking.

In conclusion, pre-exposure prophylaxis is one of the most promising HIV-prevention methods being tested, but its safety and effectiveness are unknown; even if proven safe and effective it will not be able to rid the world of HIV. However, by contrast with vaccines or **microbicides**, the drugs are already available with little need for extra manufacturing capacity. If efficacy is shown in current trials, we can expect early and possibly uncontrolled uptake from the day study results are announced. This intervention therefore needs substantial resources and infrastructure support, and pre-emptive and continued education for potential users and providers. Public-health decisionmakers need to start contingency planning now-trial results will be known soon.

Conflict of interest statement: Lynn Paxton is the coordinator of the pre-exposure prophylaxis studies sponsored by the US Centers for Disease Control and Prevention which are fully funded by the CDC. Gilead Sciences provides study drugs and placebos for these studies.

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3. PUBLISHED RESEARCH: RELEVANT BASIC AND TRANSLATIONAL SCIENCE

"Factors associated with willingness to use the contraceptive vaginal ring"

Author(s): Gilliam M, Holmquist S, Berlin A

Reference: N/A 76(1):30-4. Epub 26 May 2007.

<http://www.contraceptionjournal.org/article/PIIS0010782407001461/abstract>

Published Abstract: *Introduction:* The objective of this study was to examine factors associated with willingness to use the contraceptive vaginal ring among college students. *Material and Methods:* We electronically surveyed a random sample of female undergraduates. Factors associated with willingness to use the contraceptive vaginal ring were evaluated using a logistic regression model. *Results:* Six hundred ninety-one women answered the survey. Willingness to use the contraceptive vaginal ring was positively associated with willingness to use the contraceptive patch, being employed at least 20h/week, acceptability of a monthly contraceptive, acceptability of self-insertion, acceptability of feeling ring during intercourse and concern over potential hormonal side effects. Willingness to use the contraceptive vaginal ring was negatively associated with current use of oral contraceptives. *Discussion:* Busy lifestyle and acceptance of its characteristics were associated with willingness to use the contraceptive vaginal ring. Counseling should focus on addressing women's concerns about vaginal administration and side effects.

"HIV entry inhibitors"

Author(s): EstÃfÂ© JA, Telenti A

Reference: N/A 370(9581):81-8.

<http://www.thelancet.com/journals/lancet/article/PIIS0140673607610526/abstract>

Published Abstract: The need for new classes of antiretroviral drugs has become apparent because of increasing concern about the long-term toxic effects of existing drugs, the need to combat HIV-1 variants that are resistant to treatment, and the frequency of treatment change in drug-experienced patients. Currently, most regimens are combinations of inhibitors of two viral enzymes - reverse transcriptase and protease. Nevertheless, several steps in the HIV replication cycle are potential targets for intervention. These steps can be divided into entry steps, in which viral envelope glycoproteins and their receptors are involved, and postentry steps, involving viral accessory gene products and the cellular proteins with which they interact. New treatment options target viral entry into the cell. These treatments include the HIV fusion inhibitor enfuvirtide, and new HIV coreceptor antagonists in advanced stages of clinical development or in different stages of preclinical development. Here, we review the development of new HIV entry inhibitors, their performance in clinical trials, and their possible role in anti-HIV therapy.

"Rapid MHC-II antigen presentation of HIV Type 1 by human dendritic cells"

Author(s): Jones L, McDonald D, Canaday DH

Reference: N/A 23(6):812-6.

http://www.ncbi.nlm.nih.gov/sites/entrez?cmd=Retrieve&db=PubMed&list_uids=17604545&dopt=Abstract

Published Abstract: HIV-1 is taken up by dendritic cells (DC) and degradation is detectable within a few hours. Little is known about how rapidly HIV-peptide-loaded MHC-II complexes appear on the surface of DC, however. A key impediment to the detailed understanding of MHC-II antigen presentation of HIV-1 has been the lack of good tools to quantitatively measure antigen presentation. We have developed HIV-1-gag p24 and reverse transcriptase (RT)-specific CD4(+) T cell hybridomas that demonstrate high sensitivity and specificity to detect HIV-1 antigens presented by MHC-II on human DC. We demonstrate that ex vivo primary blood myeloid DC (mDC) and monocyte-derived DC (MDDC) presented HIV-1 peptides on MHC-II molecules within 2h of exposure to virions. HIV-1 was degraded in a compartment requiring acidification for processing and then was loaded onto newly synthesized MHC-II molecules for presentation.

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4. EPIDEMIOLOGY

"South Africa notes signs of first-ever decline in HIV infection rates"

Date: 04 July 2007

Source: *Agence France Presse*

http://news.yahoo.com/s/afp/20070704/wl_africa_afp/safricahealthaids

South Africa has seen the first-ever signs of a drop in new HIV infections, said a report released Wednesday in the country with the world's second-heaviest AIDS burden. Preliminary reports from a 2006 ante-natal survey showed HIV prevalence among pregnant women had dropped to 29.1 percent from 30.2 percent the previous year, Health Minister Manto Tshabalala-Msimang told journalists in Pretoria.

"The report indicates that this decline is mainly amongst people under the age of 20 years, followed by those between 20 and 24." The survey was carried out among pregnant women attending state clinics and hospitals, and its findings are used as an indication of the national HIV prevalence rate. "The decline in the under 20s, from 15.9 percent in 2005 to 13.7 percent in 2006, in particular, suggests a possible reduction in new infections in the population," the minister said.

The report said HIV rates have been stable for several years, adding: "This is the first evidence of a decline in the South African epidemic". South Africa recently launched an AIDS plan with the aim of reducing by 50 percent the rate of new infections by 2011, focusing on the youth among whom most new infections occur. The country has the world's second heaviest caseload of HIV/AIDS, behind India, with about 5.5 million in a population of 48 million infected, as

well as one of the world's highest rates of teenage pregnancy.

"Watch your HIV epidemic closely, warns World Bank scientist, or risk pointless prevention work"

Date: 04 July 2007

Source: *AIDSmap.com News*

Author(s): Keith Alcorn

<http://www.aidsmap.com/en/news/ADF9157F-71CC-4646-9802-827437C6A570.asp>

HIV prevention campaigns in Africa and Asia are often tilting at the wrong target and wasting money because of a basic lack of information about who is becoming infected in a country, David Wilson of the World Bank told the 2007 HIV Implementers' meeting in Kigali, Rwanda, last month. "The ABC wars have largely grown from our failure to know our epidemics," he told the conference, which was attended by around 2000 people responsible for implementing HIV treatment, care and prevention programmes in developing countries. The ABC wars refer to controversies over prevention approaches that emphasise abstinence and being faithful to partners in preference to promotion of condom use. Prevention programmes needed to recognise the difference between a concentrated epidemic and a generalised epidemic, he said.

"The conventional 1-percent [of the population] definition of generalised epidemics has hindered us knowing our epidemics". The more relevant question he argued, is: "Where did our last 1,000 HIV infections come from?" He highlighted the contrast between Uganda, where 65% of HIV infections are now estimated to take place within marriages, and Ghana, where 76% of adult male infections are linked to commercial sex workers, yet only 1% of World Bank prevention funding in Ghana goes towards work with sex workers. He also highlighted the case of Zambia, where the epidemic has moved away from the traditional vulnerable groups of sex workers, their clients, truckers and uniformed services.

"A careful study by Mark Shields suggests that only seven percent of Zambia's infections today were occurring among traditional vulnerable groups," he pointed out. "We need improved surveillance and analysis. We're not using the data we have well enough to understand our epidemics, and we have to respond more rapidly to new evidence."

Generalised epidemics - condoms are not enough

There has been controversy in some African countries about the decisions by the US government to downgrade spending on generalised condom promotion, but evidence from Uganda shows that a much more targeted approach may be required.

David Apuuli of Uganda's AIDS Commission said in an accompanying presentation that while the majority of new infections were occurring within stable partnerships in Uganda, only 14% of new infections could be attributed to casual sexual partnerships. Both mother to child transmission and sex with commercial sex workers contributed higher proportions of new infections, clearly making the case for a more targeted approach in Uganda. And as for targeting young people, "Whereas four years ago, the main new infections used to occur between 20 and 24, we now found the biggest new infections were occurring between 30 and 40," said Apuuli. "We found that discordance had gone up to

about 48% among couples from just over 22% in four years."

More than behaviour change needed

Why is HIV incidence not falling in southern Africa despite high death rates, and why is high-risk behaviour resurging in countries like Uganda? The reasons, David Wilson argued, are more to do with social environment than the sexual behaviour of individuals. In South Africa, for example, young women are at much greater risk of HIV infection than their male peers. One of the chief causes appears to be age-mixing: young women with a partner at least five years older are six times more likely to become infected with HIV, Wilson said. While the prevalence of HIV infection peaks in the 25-29 age group in women, the peak prevalence isn't reached until the age of 35 in South African men. In the Rakai district of Uganda, said Wilson, 15% of women have a coercive sexual debut and 35% have ever experienced sexual coercion, and HIV incidence is two-fold higher among women with a coercive sexual debut. It's a pattern repeated across southern and eastern Africa. Also in Rakai, alcohol abuse is associated with a 50-80% increased risk of HIV infection. Finally, concurrent sexual partnerships provide opportunities for multiple transmissions of HIV during primary HIV infection, when viral load is high. In Botswana, the country with one of the highest HIV prevalences in southern Africa, said Wilson, 43% of young men aged 15-24 reported concurrent sexual partnerships.

"What are the major lessons for generalised epidemics? Well, we have to reduce concurrency, intergenerational sex, sexual coercion, cultures of alcohol abuse and the vulnerability of couples," Wilson said. "Generalised epidemics need fundamental community change and safer sexual environments. But globally, they are the exception and will always remain the exception. And the good news is that we know what to do in concentrated epidemics."

Concentrated epidemics need condoms and clean needles

"I hope 2007 is the year we finally recognise Asia's epidemics are concentrated and focus appropriately," Wilson told the conference. "They're epidemics that are driven by vulnerable groups and initiated by sex or drugs. And the mathematics of Asian epidemics are extraordinarily robust. They are initiated by sex if we have uncircumcised men, many of whom - about 10% - routinely visit sex workers. And sex workers have large numbers of clients, typically, about 20 a week or more. And so the first wave of Asian epidemics in Thailand, Cambodia and India were sexually initiated. But elsewhere in second-wave Asian epidemics, injecting drug use has been the spark that's created sexual transmission, then sex work the motor that maintains it." He highlighted recent data from Haiphong in northern Vietnam, where HIV prevalence is 2% among sex workers who don't inject drugs and 55% among sex workers who do inject drugs. "If we dissect the figures [the wrong] way, we could easily mistake a primarily injecting epidemic for a primarily sexual epidemic," he said.

What's needed in this situation is clean needles for drug injectors and condom promotion to commercial sex workers and their clients. "But as epidemics mature and behaviour change occurs, new infections occur increasingly between infected individuals and their stable partners. And so we move from primary to secondary prevention with a far greater emphasis on testing and counselling, especially among couples. It's extraordinarily difficult to get high rates of condom use in stable unions," he said. Summing up the approach that is needed, Wilson said: "In generalised epidemics we lead with partner reduction supported by testing and counselling particularly in mature epidemics. In concentrated ones, we lead with condoms and clean needles. But many epidemics are mixed enough to need both, based on understanding of our last 1,000 infections."

5. HIV/AIDS VACCINES

"Scientific and policy challenges to development of an AIDS vaccine"

Author(s): Berkley SF, Koff WC

Reference: N/A 370(9581):94-101.

<http://www.thelancet.com/journals/lancet/article/PIIS014067360761054X/fulltext>

Published Abstract: 24 years since the identification of HIV as the causal agent of AIDS, the pandemic continues to outpace attempts at control. The response to HIV/AIDS has been inadequate, and has consisted of crisis management rather than purposeful public health policies, because of the early silent spread of the virus, its high incidence in high-risk populations, its uniformly fatal outcome if not treated, and its global proliferation. However, an unprecedented commitment to control HIV has begun. In 2005, G8 leaders agreed to provide prevention and treatment to all those in need by 2010. But, however well intended, a universal treatment paradigm is unsustainable. UNAIDS predicts that more than US\$9 billion will be needed in the next 2 years to fund AIDS treatment and care in the developing world alone. Estimates suggest that for each person who starts antiretroviral treatment, at least six people are newly infected with HIV. Thus, even if existing programmes are rapidly expanded, with increases in financing, infrastructure, and human capacity, the AIDS pandemic will continue to outpace efforts to curtail it unless we can substantially improve prevention strategies and their implementation.

If we are to control and ultimately end the pandemic, a safe, effective, practical, inexpensive, globally accessible, preventive AIDS vaccine remains the best hope. Even an AIDS vaccine with only 50% efficacy, which covered only 30% of the target population, could avert up to a third of the HIV infections that would otherwise occur, and thus save tens of millions of lives. After a burst of attention in the mid-1980s, the search for a vaccine was largely neglected in the 1990s (eg, only about \$160 million was spent worldwide in 1994). However, in the past few years investment has risen sufficiently to expand the vaccine development effort. Nearly \$800 million is spent worldwide on research and development towards an AIDS vaccine every year.

Development of an AIDS vaccine entails unique scientific challenges. The viral infection does not have many of the features that vaccinologists have traditionally used to design successful vaccines, such as induction of natural immunity to disease, known correlates of protection, and validated animal models. These novel scientific challenges demand a large-scale rational vaccine design effort, with increased and sustained financial investment in research and development, and innovative forms of scientific organisation and collaboration. Such an effort is beginning. However, we believe even greater scale, commitment, and innovation will be needed to solve the scientific questions that impede development and testing of improved vaccine candidates. We outline key scientific and policy questions that must be successfully addressed to accelerate development of a safe and effective AIDS vaccine.

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

6. POLITICS AND POLICY

"Ex-Surgeon General says White House hushed him"

Date: 11 July 2007

Source: *The Washington Post*

Author(s): Christopher Lee

http://www.washingtonpost.com/wp-dyn/content/article/2007/07/10/AR2007071001422.html?nav=rss_politics

Former surgeon general Richard H. Carmona yesterday accused the Bush administration of muzzling him on sensitive public health issues, becoming the most prominent voice among several current and former federal science officials who have complained of political interference. Carmona, a Bush nominee who served from 2002 to 2006, told the House Committee on Oversight and Government Reform that political appointees in the administration routinely scrubbed his speeches for politically sensitive content and blocked him from speaking out on public health matters such as stem cell research, abstinence-only sex education and the emergency contraceptive Plan B.

"Anything that doesn't fit into the political appointees' ideological, theological or political agenda is often ignored, marginalized or simply buried," he said. "The problem with this approach is that in public health, as in a democracy, there is nothing worse than ignoring science or marginalizing the voice of science for reasons driven by changing political winds."

In one such case, Carmona, a former professor of surgery and public health at the University of Arizona, said he was told not to speak out during the national debate over whether the federal government should fund embryonic stem cell research, which President Bush opposes. "Much of the discussion was being driven by theology, ideology, [and] preconceived beliefs that were scientifically incorrect," said Carmona, one of three former surgeons general who testified at yesterday's hearing. "I thought, 'This is a perfect example of the surgeon general being able to step forward, educate the American public.' . . . I was blocked at every turn. I was told the decision had already been made -- 'Stand down. Don't talk about it.' That information was removed from my speeches."

White House spokesman Tony Fratto rejected claims of political interference, saying Carmona had all the support he needed to carry out his mission. "As surgeon general, Dr. Carmona was given the authority and had the obligation to be the leading voice for the health of all Americans," Fratto said. "It's disappointing to us if he failed to use his position to the fullest extent in advocating for policies he thought were in the best interests of the nation."

Carmona said that when the administration touted funding for abstinence-only education, he was prevented from discussing research on the effectiveness of teaching about condoms as well as abstinence. "There was already a policy in place that did not want to hear the science but wanted to just preach abstinence, which I felt was scientifically incorrect," Carmona said. Rep. Henry A. Waxman (D-Calif.), the House panel's chairman, called for Congress to take steps to insulate the office from political influence. "We shouldn't allow the surgeon general to be politicized," he said. "It is the doctor to the nation. That person needs to have credibility, independence and to speak about science."

Carmona, a former deputy sheriff in Arizona with expertise in emergency preparedness, came to the administration's attention because of his work helping local governments plan their response to terrorist attacks. A high school dropout and former Army Special Forces medic, Carmona eventually received undergraduate and medical degrees from the University of California at San Francisco. He is the latest in a string of government employees to complain that ideology is trumping science in the Bush administration.

In January, the leader of the National Institutes of Health's task force on stem cells, Story Landis, said that because of the Bush policy -- which aims to protect three-day-old embryos -- the nation is "missing out on possible breakthroughs." And in March, NIH Director Elias A. Zerhouni called the Bush policy "shortsighted." Last year, NASA scientist James E. Hansen and other federal climate researchers said the Bush administration had made it hard for them to speak in a forthright manner about global warming. In 2005, Susan F. Wood, an assistant FDA commissioner and director of the agency's Office of Women's Health, resigned her post, citing her frustration with political interference that was delaying approval of over-the-counter sales of Plan B.

"Public health is only effective when it is honest," said David Michaels, director of the Project on Scientific Knowledge and Public Policy at the George Washington University School of Public Health. "When public health leaders don't tell the truth, they lose credibility, and in the long run, we all pay the price." Two other former surgeons general, David Satcher and C. Everett Koop, said at the hearing that political interference appears to have grown worse under Bush, although they noted that this administration has not been the only one to take a political approach toward the office.

Satcher, Carmona's predecessor, who served from 1998 to 2002, said that under President Bill Clinton he could not release a report on sexuality and public health, in part because of sensitivities triggered by the Monica Lewinsky scandal. Clinton also forced out Joycelyn Elders as surgeon general in 1994 after her controversial remarks that public schools should consider teaching about masturbation. Koop, who served as surgeon general under President Ronald Reagan, spoke out on AIDS, despite political pressure not to do so. He said Reagan was pressured to fire him every day -- but he did not. "If he had not been the kind of person he was, I would not be here today," Koop said.

"Indian minister laments country's lack of sex education"

Date: 11 July 2007

Source: *Agence France Presse*

http://news.yahoo.com/s/afp/20070711/wl_sthasia_afp/healthindiasexeducation_070711113728

India's health minister on Wednesday lamented opposition from several states to a government plan to introduce sex education from next year, a report said. "In our country, we do sex. But we don't want to talk about it and that is why we have a billion population," Health Minister Anbumani Ramadoss said at an event to mark World Population Day. "In our close-knit society, we have to enlighten and create awareness among our children," he was quoted as saying by the Press Trust of India. The government has been fighting with around a dozen out of 29 states to introduce sex education in a bid to spread awareness of AIDS and condoms as well as family planning. The Council of Boards of Education of India, which sets the teaching curriculum for schools, has prepared a package on sex education, according to a Times of India report earlier this year.

"We have recommended to make it a mandatory subject to be taught twice a week," Ramadoss said. "They will be the losers if awareness is not created at the right age," the minister said of state opposing the plan. Schools in the conservative nation, which ironically brought the world the Kama Sutra, have shied away from educating youngsters about such topics as human reproduction. But the minister said education would not provoke promiscuity. "We are not taking up sex education in a blatant manner, but in a subtle way," said Ramadoss. "We don't want to create controversy. But we have 55 per cent population that falls in the reproductive age and we have to create awareness among them."

"Thailand to launch condom campaign, implement legal protection for women whose partners refuse to use condoms"

Date: 06 July 2007

Source: *Kaiser Daily HIV/AIDS Report*

http://www.kaisernetwork.org/daily_reports/rep_index.cfm?DR_ID=46038

Thai Public Health Minister Mongkol Na Songkhla recently at Thailand's 11th annual national seminar on HIV/AIDS said he is concerned about the increasing number of HIV cases in the country, especially among married couples, the Bangkok Post reports. According to the Post, about 40% of the 18,000 new HIV cases diagnosed annually in Thailand occur among women who contract the virus from their husbands. About 28% of new cases are among men who have sex with men and 10% are among commercial sex workers, according to the Post.

Mongkol said he is considering launching a "family condom" campaign and encouraging married couples to be monogamous. "Using condoms should be regarded as showing respect to each other so that both husband and wife will be safe from sexually transmitted diseases such as HIV/AIDS," Mongkol said, adding that women also should "stand up for a better deal from their husbands."

The Thai National Committee on AIDS will carry out the condom-promotion program with Mechai Viravaidya, chair of the Population and Community Development Association. Mechai said that as part of the program, the committee will ask hotels to put complimentary condoms in guest rooms (Apiradee, Bangkok Post, 7/5). In addition, Mongkol at the seminar said that Thailand soon will provide legal protection to women whose partners refuse to wear condoms during sex, the Thai News Service reports. According to an agreement reached at a recent UNAIDS meeting in Geneva, laws on social issues and gender equality should be implemented as primary solutions to curb the spread of HIV, Mongkol said (Thai News Service, 7/5).

"Judge tells MCC to back down"

Date: 03 July 2007

Source: *News 24*

http://www.news24.com/News24/South_Africa/News/0,,2-7-1442_2140861,00.html

A Pretoria High Court judge on Tuesday accused the Medicines Control Council (MCC) of obstructing vital HIV research by the University of KwaZulu-Natal. The university's Nelson Mandela School of Medicine has been trying for more than 3½ years to get approval for an internationally funded clinical trial. The trial is to focus on the effect of Nevirapine as a prophylaxis to reduce mother-to-child HIV transmission through breastfeeding. The MCC, which maintained the clinical trial would lead to the infection of innocent babies with HIV, steadfastly refused to give heed to decisions by first an Appeal Committee and then two High Court judges, forcing it to approve the trial. The university said the delay could cause it to lose more than R47m in international donor funding, infringed on its right to academic freedom of research and aggravated the situation of HIV transmission from mother to child.

Not bound by directives

Judge Willie Hartzenberg dismissed the MCC's application on Tuesday for leave to appeal against a court ruling, ordering it to immediately approve the clinical trial, even although an appeal was pending. Judge Hartzenberg criticised the MCC for deliberately delaying matters and being "obstructive" in an attempt to have the application "disappear". The MCC also seemed to adopt the attitude that it was not bound by directives given by the court. There could not be any objection against the clinical trial based on the use of Nevirapine, which has been registered by the MCC and has been found to be safe, said the judge. He said it was clear the Appeal Committee had been "very alive" to the ethical objections to the clinical trial, where one half of HIV-positive breastfeeding mothers would get Nevirapine, and the other would get placebos.

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7. HIV/AIDS FUNDING

"Henan sets up NGO for AIDS prevention"

Date: 09 July 2007

Source: *Xinhua News Agency*

Author(s): Lin Li

http://news.xinhuanet.com/english/2007-07/09/content_6350634.htm

Central China's Henan Province, which has the second highest number of HIV/AIDS cases in the country, set up on Monday a non-governmental AIDS prevention and treatment organization. The Henan AIDS Prevention and Treatment Association will play an active role in AIDS prevention education and help those infected with the disease, said Huang Wei, chairman of the non-governmental organization. At the end of 2006, Henan had reported 35,232 HIV cases, the second biggest total after southwest China's Yunnan Province, which had 48,951 cases. The majority of the infections in Henan were caused by illegal or poorly controlled blood trade in the 1990s. The association will seek domestic and international partners to help with AIDS prevention funding and programs, said Huang, also deputy director of the Henan provincial health department. The organization has 137 members, including HIV carriers, AID patients, teachers, lawyers, journalists and entrepreneurs. Some Chinese provinces plagued by AIDS have already established associations for prevention and treatment of both venereal disease and AIDS.

"Human virology institute gets \$43 million federal grant"

Date: 09 July 2007

Source: *Associated Press*

http://www.examiner.com/a-819470~Human_virology_institute_gets__43_million_federal_grant.html

The Institute of Human Virology at the University of Maryland School of Medicine has received a \$43 million federal grant to help fight AIDS in Nigeria. The money from the President's Emergency Plan for AIDS Relief will be used to treat 48,000 patients in Nigeria and to expand HIV testing and counseling to an additional 100,000 people, the university announced Monday in a release. The institute's AIDS Care and Treatment in Nigeria, or ACTION, was founded in 2003 using a model where members of the institute's medical team work with Nigerian colleagues to get communities involved in treatment and care. ACTION has placed thousands of Nigerians on therapy and provided thousand so of pregnant women in the country with HIV preventive services. "The work being done now in Nigeria is extraordinary," Dr. Robert C. Gallo, the founder and director of IHV, said in a statement. "This new award enables us to reach even more people who need the care and treatment provided by our institute's experts," Gallo said.

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8. ANNOUNCEMENTS

Deadline for abstracts to **Microbicides 2008**

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

Per an informational email from **Microbicides 2008**, the Alliance has learned that Abstracts for the conference are due by 30 September, 2007. This date has not yet been posted on the **Microbicides 2008** website, and further information for abstracts is still unavailable. However, we encourage the community to begin thinking about abstracts for this very important conference! Below is an excerpt from the **Microbicides 2008** website:

"**Microbicides 2008** is a wonderful opportunity to showcase your research, your work and your support for the ongoing efforts to develop safe and accessible **microbicides** and we encourage you to submit your abstracts. We assure you that you would enjoy the conference in the beautiful city of New Delhi and hope that the interactions and experience of the conference will renew your efforts in this critical field of HIV prevention."

IAS releases Sydney Declaration, calls for increase in research funding to fight HIV/AIDS

http://www.kaisernetwork.org/daily_reports/rep_index.cfm?DR_ID=46098

EDITOR'S NOTE: Alliance for Microbicide Development has signed the Sydney Declaration, and we encourage our colleagues and others in the community to do the same. Please read below for more information.

The International AIDS Society on Tuesday ahead of the 4th IAS Conference on HIV Pathogenesis, Treatment and Prevention -- scheduled to take place July 22 to July 25 in Sydney, Australia -- released the Sydney Declaration, which calls for increased research funding to fight HIV/AIDS worldwide, the Australian Associated Press reports.

The declaration proposes that donors allocate at least 10% of their HIV resources to research and states that "although funding remains insufficient to meet the increasing need for services, it is imperative that the global community does not lose sight of the future while responding to the immediate crisis."

The declaration notes that "in addition to basic, clinical, prevention, social, and policy research," operations research also is important to "enable rapid implementation of new technologies to prevent, diagnose and treat" HIV (McLean, Australian Associated Press, 7/10). Few countries and organizations allocate funds for research and often do not use such funding when it is available, the declaration says. According to the declaration, the Global Fund To Fight AIDS, Tuberculosis and Malaria allows 10% of each grant for operations research, but the provision rarely is used by countries (Sydney Declaration, July 2007).

IAS in a statement released with the declaration said that "without such funding," the international community will "fail to maintain a sustained and effective response to the AIDS pandemic." David Cooper, director of Australia's National Centre for HIV Epidemiology and Clinical Research, said the funding pledge is critical to address HIV in developing countries and ensure that HIV prevention and treatment programs are integrated with existing health programs, such as hospital care and TB, malaria, prenatal, postnatal, and sexual and reproductive health services (Australian Associated Press, 7/10).

The declaration also called for a "sustained commitment" to continuously improve evidenced-based HIV services and for a "greater understanding" of the social, political and cultural barriers that contribute to stigma and discrimination associated with HIV. In addition, the declaration addressed the "absurd theories of AIDS denialists" and "'magic cures" that "continue to confuse policymakers, health care professionals and communities of people at risk of and living with HIV/AIDS throughout the world" (Sydney Declaration, July 2007).

Safety of new microbicide for HIV prevention

<http://www.mtnstopshiv.org/downloads/mtn004/faq/MTN-004%20release%20final.pdf>

The **Microbicide** Trials Network (MTN) is leading the National Institutes of Health-funded study in which SPL7013 Gel, or VivaGel[®], is being tested for the first time in sexually active young women to determine the product's safety, acceptability and ease of use. The expanded safety study, known as MTN-004, is being conducted at the University of South Florida in Tampa and the University of Puerto Rico in San Juan through a collaboration between the MTN, an HIV/AIDS clinical trials network established by the National Institute of Allergy and Infectious Diseases, and the Adolescent Medicine Trials Network for HIV/AIDS Interventions (ATN) of the National Institute of Child Health

and Human Development.

VivaGel is thought to act by hampering the ability of HIV to attach to and infect healthy cells. Unlike other candidate **microbicides**, including those that target similar cell mechanisms, the active ingredient of VivaGel, belongs to a class of compounds called dendrimers. A dendrimer is a large molecular structure that incorporates multiple units of an active component on its surface. In the case of SPL7013, each dendrimer incorporates 32 copies of the active component. Starpharma Pty.Ltd., of Melbourne, Australia, is developing VivaGel for the prevention of both HIV/AIDS and genital herpes.

The MTN-004 study will enroll 40 sexually active, HIV-negative women between the ages of 18 and 24 years of age. Participants will be randomly assigned to one of two study groups, with neither the researchers nor the participants knowing their assignment. One group will apply VivaGel twice a day for two weeks, while participants in the other group will apply a placebo gel with no active ingredients. All women in the study will be provided condoms to be used with each act of sex. Researchers will assess the safety of VivaGel compared with the placebo gel through laboratory tests and regular clinical examinations of study participants. Web-based questionnaires will also provide information about the product's acceptability, such as what participants liked or disliked about using the gel, how their sexual partners felt about its use and how likely they are to use **microbicides** in the future. Participation in the study will last three weeks, including the two-week period that gels are used.

EDITOR'S NOTE: This announcement is compiled from excerpts of MTN's Press Release on 9 July 2007. To view the full Press Release, please visit the above website.

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