



# ALLIANCE FOR MICROBICIDE DEVELOPMENT

**20 April 2007, Volume 8, Number 15**

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

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

Its purpose is to:

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

The *News Digest* is produced in a web-based format. Readers can view individual articles or complete issues at <http://www.microbicide.org/publications/> and may also search by keyword for articles included in issues of the *Digest* created after 27 January 2006, at <http://www.microbicide.org/publications/search.html>. Should you wish to be removed from the *Digest* distribution list, please advise us at [digest@microbicide.org](mailto: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

#### New article and interview from Women Matter

<http://www.womenmatter.com/healthcare/index.htm>

Women Matter, a "content-driven, nonpartisan web-based organization that is designed to educate women about political processes and help them to use those processes to better their own lives," is featuring an article on **microbicides**, "Protect yourself: new possibilities for women in the bedroom" on their website. The article, which can be found at [http://www.womenmatter.com/health\\_whatnew20070403.htm](http://www.womenmatter.com/health_whatnew20070403.htm) covers women's need for tools like **microbicides**; basic information about **microbicides** and the drug development process; the status of **microbicide** development and funding; the ethical challenges of conducting **microbicide** clinical trials; and the **Microbicide** Development Act and other current legislation. The site also features a 12-minute interview with Dr. Polly F. Harrison, Director of the Alliance. The interview can be found at <http://www.womenmatter.com/healthcare/index.htm>

#### Special Alliance Announcement

The Alliance wishes to inform you that Dr. Franka des Vignes will be leaving the Alliance at the end of May 2007 to relocate to Trinidad and Tobago. Franka has been with the Alliance since July 2002 and has contributed tremendously during her time with us. We are extremely grateful for the nearly five years that she has spent at the Alliance, and we

will miss her as a colleague and friend. While we are saddened by Franka's departure, we are happy to know that the relocation will allow her to be closer to her family and to continue her career as an infectious disease epidemiologist. Please join us in wishing Franka all the best in her new endeavors!

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## 2. MEDIA COVERAGE OF MICROBICIDES

### "German researchers find protein that blocks HIV"

**Date:** 20 April 2007

**Source:** *The San Francisco Chronicle*

**Author(s):** Sabin Russell

<http://www.sfgate.com/cgi-bin/article.cgi?file=/c/a/2007/04/20/MNGHKPC9381.DTL>

German researchers have opened a door to a potential new AIDS drug with the discovery of a small protein circulating in human blood that blocks multiple strains of HIV, even those resistant to existing medications. This natural anti-HIV factor -- a chain of 20 amino acids known as a peptide -- interferes with a feature on the surface of the AIDS virus that otherwise allows the virus to penetrate the membrane of cells it is about to infect, a process known as fusion.

University of Ulm researcher Frank Kirchhoff and colleagues found the peptide in the residue left in filters used by kidney dialysis patients to cleanse their blood. These filtrates have proved to be a rich source of biological agents because they are derived from high volumes of blood carrying an astonishing variety of peptides, proteins and other factors whose functions are often unknown. "The big advantage of this source is that it is available in huge quantities," Kirchhoff said in a telephone interview from Germany. In addition to toxins and waste material strained from blood, the dialysis filtrates contain more than a million molecules.

Kirchhoff calls the newly discovered factor VIRIP, and it was shown in test-tube studies to inhibit 60 strains of HIV. His study describing the peptide was released Thursday by the journal *Cell*.

After discovering the peptide's anti-HIV properties, the researchers began to tinker with it. By changing just two amino acids, they increased its antiviral potency a hundredfold, Kirchhoff said. That peptide, which can be manufactured in a lab, has been licensed to a German biotech company, Viro Pharmaceuticals GmbH, whose scientific director is a co-author of the paper.

The German company is conducting animal studies of VIRIP to determine if it is safe to test in humans. "So far, the results look promising," Kirchhoff said, although it will take five or more years of success in animal and human clinical trials before the drug could be ready to market. Since the 1980s, dozens of AIDS drug candidates that performed well in initial studies have failed to pass muster in rigorous and large-scale trials.

Dr. Warner Greene, director of the Gladstone Institute of Virology and Immunology in San Francisco, said that this particular drug candidate stands out because it was gleaned from human blood. "I thought it was a masterful piece of work," he said. "They've identified a naturally occurring peptide that has antiviral activity, then they figured out how it works." It was particularly ingenious, he said, for the researchers to tap the kidney dialysis waste as a potential source

of active biological agents. "They decided to mine it. They could have struck out, but they struck gold," he said.

Greene said the peptide might work synergistically with Fuzeon, commonly called T-20, an injectable drug approved in 2003 and used by AIDS patients who have burned through just about every other available antiviral medication. Like T-20, the VIRIP attacks a protein known as GP-41 on the surface of HIV. Also like T-20, the new peptide could offer hope to patients on "salvage therapy" who are running out of treatments that can keep them alive.

Scientists have deduced with remarkable precision just how GP-41 stabs into the surface of human cells, prying open a hole for the rest of the AIDS virus to slip in. The fusion process requires multiple steps in which GP-41 changes its shape, operating at times like a spring, spear or lever. Interfering with any one of those steps could block HIV infection. T-20, the only fusion-inhibitor on the market, attacks a late step in the fusion process. VIRIP, the new research shows, interferes earlier.

Because the peptide blocks HIV infection before the virus can enter a cell, Greene said that it is possible that VIRIP has potential as an active ingredient for a **microbicide** -- a vaginal cream or gel that women could apply to protect themselves from the AIDS virus.

Nevertheless, because VIRIP is a peptide -- a larger and more complex structure than drugs made up of chemical compounds -- it will always be more costly to make and probably will have to be injected with a hypodermic. T-20 has not emerged as a blockbuster AIDS drug because it is costly -- about \$25,000 for a year of treatments -- and requires injections that can cause painful skin reactions. "A peptide is obviously not ideal," Kirchhoff agreed. He hopes that further research will reveal how a smaller chemical compound could be designed that would work the same way and perform just as well as VIRIP. "In the long run, we must go away from peptides," he said.

### "More information on the Brazilian algae candidate"

**Date:** 31 March 2007

**Source:** CBAS Newsletter

<http://www.cervicalbarriers.org/newsletter/#Brazil>

On January 16, BBC News Online reported that Brazilian researchers had found a candidate **microbicide** that was 95% effective in laboratory tests. The report then noted that, "First-generation **microbicides** now being tested are expected...to be 50 - 60% effective. However, preliminary tests of the Brazil gel suggest it could be substantially more effective."

While news of any new **microbicide** candidate is exciting, this report may have implied a bigger breakthrough than actually occurred. Pre-clinical (laboratory) testing is a first step in product development and candidates are not advanced to the next steps unless they show strong indications of potential effectiveness. However, a compound must clear many more tests before it enters human trials as a candidate **microbicide**.

Dr. Luiz Castello Branco, an immunologist at the well-regarded Oswaldo Cruz Institute in Rio de Janeiro and Principal Investigator of this compound, shared the following information with our colleagues at the **Alliance for Microbicide Development**. The compound is dolabellane diterpene isolated from the marine algae *Dictyota pfaflii*. In the test tube, it appears to inhibit HIV-1 reverse transcriptase and HIV-1 replication at a post-transcriptional step.

One journal article on their findings has been published and a second one is in press. Dr. Branco's team believes that the potentially inflated news of their results was generated by the media and may have arisen from a misunderstanding of the original news coverage in Portuguese.

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### 3. PUBLISHED RESEARCH: MICROBICIDE-SPECIFIC

#### "Entry inhibitor-based microbicides are active in vitro against HIV-1 isolates from multiple genetic subtypes"

**Author(s):** Ketas TJ, Schader SM, Zurita J, et al

**Reference:** N/A Epub ahead of print.

[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list\\_uids=17428517&query\\_hl=5&itool=pubmed\\_docsum](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=17428517&query_hl=5&itool=pubmed_docsum)

**Published Abstract:** Inhibitors of viral entry are under consideration as topical **microbicides** to prevent HIV-1 sexual transmission. Small molecules targeting HIV-1 gp120 (BMS-378806) or CCR5 (CMPD167), and a peptide fusion inhibitor (C52L), each blocks vaginal infection of macaques by a SHIV. A **microbicide**, however, must be active against multiple HIV-1 variants. We therefore tested BMS-C (a BMS-378806 derivative), CMPD167, C52L and the CXCR4 ligand AMD3465, alone and in combination, against 25 primary R5, 12 X4 and 7 R5X4 isolates from subtypes A-G. At high concentrations (0.1-1 µM), the replication of most R5 isolates in human donor lymphocytes was inhibited by >90%. At lower concentrations, double and triple combinations were more effective than individual inhibitors. Similar results were obtained with X4 viruses when AMD3465 was substituted for CMPD167. The R5X4 viruses were inhibited by combining AMD3465 with CMPD167, or by the coreceptor-independent compounds. Thus, combining entry inhibitors may improve **microbicide** effectiveness.

#### "HIV-1 subtype A envelope variants from early in infection have variable sensitivity to neutralization and to inhibitors of viral entry"

**Author(s):** Blish CA, Nedellec R, Mandaliya K, et al

**Reference:** N/A 21(6):693-702.

[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list\\_uids=17413690&query\\_hl=5&itool=pubmed\\_docsum](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=17413690&query_hl=5&itool=pubmed_docsum)

**Published Abstract:** BACKGROUND: An effective HIV-1 vaccine or **microbicide** must block the transmitted virus variants that initially establish a new infection; consequently, it is critical that such viruses be isolated and characterized. OBJECTIVE: To evaluate HIV-1 envelope variants from early in infection from individuals infected heterosexually with subtype A HIV-1 for their sensitivity to antibody-mediated neutralization and to inhibitors of viral entry. METHODS: Full-length subtype A HIV-1 envelope clones from 28-75 days postinfection were used to generate pseudoviruses for infection studies. The susceptibility of these pseudoviruses to neutralization by autologous and

heterologous plasma and by monoclonal antibodies was examined. The sensitivity of these pseudoviruses to PSC-RANTES and TAK-779, inhibitors of CCR5, and to soluble CD4 (sCD4) was also evaluated. RESULTS: Pseudoviruses with subtype A HIV-1 envelopes from early in infection demonstrated a broad range of neutralization sensitivities to both autologous and heterologous plasma. However, neutralization by the monoclonal antibodies b12, 2G12, 4E10 and 2F5 was generally poor; notably, none of the 14 early virus variants were neutralized by 2G12 and only one was neutralized by b12. Viruses bearing these early CCR5-using envelopes were generally sensitive to the CCR5 inhibitors PSC-RANTES and TAK-779, but they demonstrated more variable sensitivity to sCD4. CONCLUSIONS: These subtype A HIV-1 variants, representing the viruses that must be blocked by antibody-based prevention strategies, vary in their susceptibility to neutralization. A subset of these HIV-1 variants from early in infection will be useful for screening candidate vaccines and **microbicides**.

### "Limitations of the Human-PBL-SCID mouse model for vaginal transmission of HIV-1"

**Author(s):** D\Cruz OJ, Uckun FM

**Reference:** N/A 57(5):353-60.

[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list\\_uids=17430499&query\\_hl=2&itool=pubmed\\_docsum](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=17430499&query_hl=2&itool=pubmed_docsum)

**Published Abstract:** Problem: SCID mice reconstituted with human peripheral blood lymphocytes (PBL) are amenable to vaginal transmission of HIV-1. We investigated the effectiveness of this model to establish systemic HIV-1 infection. Method of study: Eighty progesterone-primed C.B-17 SCID mice were reconstituted with human-PBLs and intravaginally inoculated with CCR5 HIV-1 (BaL or 92BR09) infected human-PBLs in the presence of human semen. After two weeks, viral RNA load in spleen, peritoneal lavage (PL), and serum was quantitated by the nucleic acid sequence-based amplification method. Results: In five independent experiments, spleen from 8/60 (13.3%), PL from 7/60 (11.6%), and serum from 16/56 (28.5%) mice were positive for BaL HIV-1 infection. Similarly, spleen from 4/20 (20%), PL from 1/20 (5%) and serum from 5/20 (25%) mice vaginally inoculated with 92BR09-infected human-PBLs were positive for HIV-1. A one-sided power analysis using normal approximation revealed that at 5% significance level, the overall response rate need to increase from 0.29 to 0.9 and 80% of the control groups needs to achieve a response rate between 6/10 and 9/10 to make the assay feasible. Conclusion: The incidence of vaginal transmission of CCR5 HIV-1 in the human-PBL-SCID mouse was low and variable, which constitutes a major disadvantage for preclinical evaluation of vaginal **microbicides**.

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## 4. PUBLISHED RESEARCH: RELEVANT BASIC AND TRANSLATIONAL SCIENCE

### "Predictors of dual method use for pregnancy and HIV prevention among adolescent South African women"

**Author(s):** Macphail C, Pettifor A, Pascoe S, et al

**Reference:** N/A 75(5):383-9.

[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list\\_uids=17434021&query\\_hl=8&itool=pubmed\\_docsum](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=17434021&query_hl=8&itool=pubmed_docsum)

**Published Abstract:** INTRODUCTION: Dual contraceptive method use is advocated for adolescent women to prevent pregnancy, sexually transmitted diseases and HIV. METHODS: We examined data from a nationally representative sample of South African women aged 15-24 years to establish factors associated with dual method use. RESULTS: Only 7% of current contraceptive users reported using dual methods, although this percentage increased to 28.1% when women reporting hormonal contraception and condom use at last sex were included. In multivariate analyses, having talked about condoms with a partner was most strongly associated with dual method use (adjusted odds ratio (AOR), 12.3; 95% confidence interval (CI), 6.1-25.1) and suggests that communication skills might be the most effective way of increasing dual method use. Difficulty in accessing condoms was associated with lower odds of dual method use (AOR, 0.5; 95% CI, 0.2-1.0). CONCLUSION: We conclude with recommendations to increase male involvement and encourage communication between partners for the integration of HIV prevention and other reproductive health care services.

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## 5. OTHER PREVENTION APPROACHES

### "Inconsistent condom use by UK's gay men, with many putting themselves or others at risk of HIV"

**Date:** 19 April 2007

**Source:** *AIDSmap.com News*

**Author(s):** Michael Carter

<http://www.aidsmap.com/en/news/51CC5AD0-D3EF-440B-9602-4B4A26DF076A.asp>

Approximately 50% of sexually active gay men in the United Kingdom had unprotected anal sex in the last year, according to the results of the 2005 Gay Men's Sex Survey, *Consuming Passions*, which has been published by Sigma Research. The survey also revealed that over 40% of gay men in the UK are unaware of their own HIV status and most sexual encounters occur between men who have not disclosed their HIV infection status.

The study showed in no uncertain terms that a significant amount of sexual activity was taking place that involved a very real risk of HIV transmission. Specifically, it was shown that approximately one-third of HIV-positive men (rising to over 50% of men with large numbers of partners) had had unprotected insertive anal sex with a man who was either HIV-negative or of unknown HIV status; that almost 20% of HIV-negative men had had receptive unprotected anal sex with a man of unknown HIV status, as had approximately a fifth of untested men (rising to 30% of untested men with the greatest numbers of partners).

Some myths about the causes of sexual risk taking were also dispelled by the survey. There has long been an assumption that gay men have low self-esteem, partly related to feelings about their attractiveness, and leading to risky sex. However, few men in the survey reported rating their attractiveness as below average, and HIV-positive

men were the most likely to rate their looks as better than the norm.

The ninth Gay Men's Sex Survey was completed by almost 16,500 men in the summer and early autumn of 2005.

#### *Large numbers remain untested*

Large numbers of gay men remain untested for HIV in the UK, with 44% of those completing the survey saying that they had never had an HIV test. Of the men who reported testing negative, 56% had done so in the last year.

Although only 7% of the entire sample said they were HIV-positive, this rose to 12% when the investigators restricted their analysis to men who had had a test. Some of the HIV-positive men had been living with the infection for 20 years, but approximately 50% of all men with HIV had had their infection diagnosed within the last five years.

Unsurprisingly, HIV prevalence was highest amongst gay men in London, (12% versus 4% elsewhere in the UK), but the proportion of men recently testing positive was similar across the country at approximately 4%. Although younger gay men have often been viewed as a group particularly vulnerable to HIV infection, the study revealed that the age group with the highest proportion of infections in the last year was 35 - 39.

#### *Recent sexual activity*

Almost all the men (94%) said that they had had sex with another man in the previous twelve months, with 48% of men said that they had between two and twelve partners over the last year, and 11% reporting 30 or more partners.

Because unprotected anal sex is the sexual activity that involves the greatest risk of HIV transmission, a large part of the survey was devoted to establishing the level of recent condom use by gay men, the reported HIV status of unprotected sex partners, and levels of, and factors associated with, condom failure.

#### *Over half of gay men reporting anal sex report inconsistent or no condom use*

Insertive anal intercourse was reported by 74% of men. Of these men, 48% said they always used a condom, 39% said they sometimes used a condom, and 13% said they never used a condom. Of the 70% of men who reported receptive anal intercourse, 46% said they always used a condom, 40% said they sometimes used a condom, and 14% reported never using a condom.

When asked directly about their condom use for anal sex, 39% of the entire sample reported inconsistent use for insertive anal sex, and 38% of all men said that they sometimes or never used condoms for receptive anal sex.

Although HIV-positive men were the group most likely to report any condom use, they were also most likely to report inconsistent condom use.

#### *Unprotected sex with men of different or unknown HIV status*

The overwhelming majority of HIV-positive men (79%) said that they had had no unprotected anal sex with men who they knew to be HIV-negative, however, 46% reported having anal sex without a condom with men who were also HIV-positive, and 43% said that they had had unprotected sex with men whose HIV status they did not know.

Only 4% of HIV-negative men said that they had had unprotected sex with a man they knew to be HIV-positive, although approximately a third of HIV-negative men reported risky sex with a man whose HIV status they did not know. Of the untested men, only 1% reported unprotected sex with a man they knew to be HIV-infected, with over a quarter saying that they had anal sex without a condom with a man whose HIV status was unknown to them.

Despite these efforts to minimise the risk from unprotected anal sex, the survey did show that significant numbers of men were engaging in sexual activity that could involve the risk of HIV transmission: 29% of HIV-positive men (rising to over 50% of men with 30 or more sexual partners) reported unprotected insertive anal sex with a man of unknown HIV status in the last year; 19% of negative men reported receptive anal sex with a man of unknown HIV status in the last year; and, 19% (rising to a third of the those with 30 partners or more) of untested men had receptive anal sex without a condom in the previous twelve months with a man whose HIV status they did not know.

#### *Factors associated with risky sex*

Factors significantly associated with HIV-positive men having unprotected insertive sex with men who were either HIV-negative or of unknown HIV status were: being in a serodiscordant or unknown status relationship; having 30 or more sexual partners; rating attractiveness as better than average; and drug use (all  $p < 0.05$ ).

HIV-negative men having unprotected receptive sex with men who were HIV-positive or unknown HIV status were significantly more likely to: live in southern England or Wales; be aged under 20 or over 50; be black British or white British; have less or no education post-16; to earn less than £20,000 a year; to be in a serodiscordant relationship or in a relationship with a man whose HIV status they did not know; to have had 30 or more sexual partners in the last year; and to use drugs (all  $p < 0.05$ ).

#### *Condom failure*

The survey also sought to establish the proportion of men who had experienced condom failure (for example, slippage or breakage) in the last year. Of the men who had used condoms, 13% said that they had failed in some way.

Condom failure was significantly associated with inconsistent use. Other factors associated with condom problems were anal sex for 30 minutes or more; the use of either no lubricant or saliva or a non-water based lubricant; using an inappropriately sized condom; younger age; lack of an education post 16; lower annual income; being a practicing Muslim; having sex with men of unknown or different HIV status; having 30 or more sexual partners a year; and drug use.

#### *Attractiveness*

Low self-esteem has for many years been seen as one of the reasons why gay men take sexual risks. Some health promoters had expressed concern that men who have a poor perception of their attractiveness are likely to engage in HIV risk behaviours.

However, the survey found that most gay men (51%) thought that they were as attractive as men of the same age, and that 37% thought they were either somewhat more attractive than the average or much more attractive than average. Only 12% of men thought they were either less, or somewhat less attractive than average.

The study found that HIV-positive men were more likely than either HIV-negative or untested men to rate their attractiveness as higher than average. Furthermore, HIV-positive men who thought of themselves as attractive were more likely to have unprotected insertive anal sex with men who they knew to be HIV-negative or whose HIV status they did not know. Unsurprisingly, the survey also found that men who rated their attractiveness highly had the greatest number of sexual partners.

#### *Where now?*

The authors recommend that interventions should be targeted at so called 'naive risk taking' - men having unprotected sex with men whose HIV status is unknown. Men with large numbers of sexual partners should be a special focus of

such interventions.

Health promotion campaigns should also, the authors recommend, be targeted at men who know that their partners are of a different HIV status, particularly if they have large numbers of partners.

#### Reference

Hickson, F et al. Consuming passions: findings of the United Kingdom Gay Men's Sex Survey 2005. Sigma Research, 2007.

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## 6. POLITICS AND POLICY

### "Abstinence-only sex education report should be 'bridge' between policy extremes, editorial says"

**Date:** 18 April 2007

**Source:** *Kaiser Daily Womens Health Policy Report*

[http://www.kaisernetwork.org/daily\\_reports/rep\\_index.cfm?DR\\_ID=44332](http://www.kaisernetwork.org/daily_reports/rep_index.cfm?DR_ID=44332)

Two newspapers recently published editorials responding to a report on sex education that found that abstinence-only sex education programs are not effective in preventing or delaying teenagers from having sexual intercourse. The report, commissioned by Congress and released on Friday by Mathematica Policy Research, followed 2,057 U.S. teenagers in late elementary and middle school who participated in four abstinence programs, as well as students in the same grades who did not participate in such programs. About half of the students who received abstinence education and about half of those who did not reported that they abstained from sex. More than one-third of both groups had two or more sexual partners; 23% of both groups reported having had sex and always using a condom; 17% of both groups reported having had sex and only sometimes using a condom; and 4% of the students in both groups reported having had sex and never using a condom, according to the report (*Kaiser Daily Women's Health Policy Report*, 4/16). Summaries appear below.

- *Boston Globe*: Abstinence "should be part of the message that young people hear about sex," but "as a protection against sexually transmitted [infections] and unplanned pregnancies, the abstinence message goes only so far," a *Globe* editorial says. "Congress should drop its abstinence-only programs and encourage communities to offer comprehensive sex education that includes information on diseases and the various methods of contraception" in light of the study, the editorial says. The *Globe* says that Congress also should require a "rigorous" study of the Bush administration's abstinence-based HIV prevention programs in Africa and the Caribbean (*Boston Globe*, 4/18).
- *Washington Post*: The report should serve as "a bridge between the two extremes of the sex education debate," a *Post* editorial says. "What's needed" are programs that encourage teens "to delay having sex until they are ready to handle the risk and responsibility and that encourage sexually active youths to use contraception," according to the *Post*. "The Bush administration should consider using some of the \$176 million it spends on abstinence education to foster more" programs that "deal with the real world" instead of "poo-hooing the latest evidence that its efforts will not have the promised impact," the editorial concludes (

## "AIDS drugs reach more people, U.N. report says, but not enough"

**Date:** 18 April 2007

**Source:** *The New York Times*

**Author(s):** Lawrence K. Altman

<http://www.nytimes.com/2007/04/18/health/18aids.html?ex=1177560000&en=588b230b6ecedc08&ei=5070&emc=eta1>

About two million people in the world are receiving drugs for AIDS, an increase of 700,000 in the last year, the United Nations said in a report issued yesterday. But the two million total is a million less than the three million people that the World Health Organization had hoped would be receiving treatment by the end of 2005. It represents only 28 percent of the 7.1 million people with advanced AIDS who need such therapy in poor and middle-income countries. Still, the effort is "a remarkable success" considering that only 2 percent of infected patients needing antiretroviral therapy were receiving it three years ago, said Dr. Kevin De Cock, the H.I.V./AIDS director at the World Health Organization, a United Nations agency in Geneva.

Countries in every area of the world are making substantial progress in scaling up efforts, he said. Studies show that survival rates were about 93 percent after one year among people starting antiretroviral therapy in developing nations, a rate that is similar to those in the United States and other rich countries, Dr. De Cock told reporters by telephone. Studies have also shown that levels of immune cells known as CD-4 were similar to those in rich countries, as was the drop in the amount of H.I.V., the virus that causes AIDS, in the blood. But many numbers were discouraging. In 2006, about six times as many people became infected with H.I.V. as started treatment, meaning prevention efforts are faltering or not in place, Dr. De Cock told reporters by telephone.

In 2003, only 400,000 people were being treated. So when the World Health Organization set an ambitious goal of treating three million infected people by the end of 2005, the plan met with enormous skepticism. Though the numbers achieved are smaller than desired, those receiving therapy are benefiting, Dr. De Cock said. "If you visit these countries, go to clinics and go to people's houses, you see people going back to work," Dr. De Cock said. "It is pretty impressive."

More governments must issue specific plans on how they will achieve greater success in preventing and treating AIDS, the report said. More than 150 countries committed themselves to setting targets for universal access to treatment by the end of 2006. But only 90 have provided data on such plans by that date, the report said.

The report recognized that preventing and treating AIDS was a complex problem hampered by weak health systems in poor countries. But the United Nations urged governments to do more to provide relatively simple antiretroviral regimens to mothers to prevent transmission of the virus to their infants. Only 11 percent of pregnant women in developing countries are receiving such therapy now, the report said.

Better tests and improved drug formulations are needed to treat children, and better care is needed for injecting drug users who are at high risk of becoming infected with H.I.V.

Although prices for the standard antiretroviral drugs have fallen, health officials are concerned about the high costs of second-line, or backup, drugs that are needed when the first-line drugs fail.

The report urged greater efforts to control tuberculosis because nearly a million people with H.I.V. develop tuberculosis each year, leading to about a quarter of a million deaths.

The Bush administration's emergency plan for AIDS Relief and the Global Fund to Fight AIDS, Tuberculosis and Malaria were paying for care of about 1.27 million of the two million total, the United Nations said.

### **"Gates Foundation billions change pharma landscape"**

**Date:** 17 April 2007

**Source:** *Reuters*

**Author(s):** Ben Hirschler

[http://news.yahoo.com/s/nm/20070417/hl\\_nm/gates\\_pharmaceuticals\\_dc](http://news.yahoo.com/s/nm/20070417/hl_nm/gates_pharmaceuticals_dc)

The billions of dollars thrown at global health problems by the Bill & Melinda Gates Foundation are changing the game in drug discovery, posing big challenges to the world's top drugmakers, according to a report on Tuesday. Pharmaceutical information group IMS Health Inc. said the emergence of megabuck philanthropy was both a threat and a collaboration opportunity for manufacturers. "Pharma companies need to develop an explicit strategy to deal with this phenomenon," IMS said in its annual Intelligence.360 report on factors shaping the industry.

The power of the Gates Foundation was bolstered last year when Warren Buffett signed over much of his fortune to the organization, uniting the world's two richest people in a bid to fight disease, reduce poverty and improve education. The move will roughly double the foundation's size to \$60 billion, giving it plentiful resources to compete in the medical research arena with both government-funded institutions and commercial pharmaceutical firms. As a result, even if drug companies succeed in making key discoveries first, they may still find it attractive to partner with the Gates Foundations, from a practical and public relations point of view, IMS believes.

#### *AIDS Vaccine*

A \$287 million grants program announced last July -- creating an international network of 16 labs to try new approaches to making a vaccine against AIDS -- exemplifies the ground-breaking approach pioneered by the foundation. It aims to transform the so-far unsuccessful AIDS vaccine effort by rewarding individual labs that come up with innovative ideas and helping them develop those ideas, while also ensuring they collaborate with rivals.

To get quick results, the new Collaboration for AIDS Vaccine Discovery may need to access and use patented compounds still under development at pharmaceutical and biotech firms, IMS said. That will

raises fresh debate over the ethics surrounding patents on life-saving AIDS drugs and vaccines -- of which there are more than 200 in development. Leading makers of AIDS drugs include GlaxoSmithKline Plc and Merck & Co. Inc., both of which are also working to develop vaccines.

Drugmakers, in future, could face mounting pressure to collaborate with the foundation, even if this impacts their bottom line. "Whether or not the Gates Foundation effort succeeds, it benefits pharma companies to stay in the game, working synergistically with the foundation," IMS said. "The alternative is for pharma to allow itself to be perceived as indifferent to global health concerns -- or to be unseated in the pursuit of advances in world health."

Bill Gates, the world's richest person, co-founded and remains chairman of software company Microsoft Corp., while Buffett built the world's second-biggest personal fortune running Berkshire Hathaway Inc., an insurance and investment company.

### **"Preventing H.I.V., but at what price?"**

**Date:** 15 April 2007

**Source:** *The New York Times*

**Author(s):** Donald G. McNeil Jr.

[http://www.nytimes.com/2007/04/15/weekinreview/15mcneil.html?\\_r=2&oref=slogin&oref=slogin](http://www.nytimes.com/2007/04/15/weekinreview/15mcneil.html?_r=2&oref=slogin&oref=slogin)

Read the next sentence aloud, and watch all the men around you involuntarily cross their legs: How do you persuade a grown man to get circumcised? Answer: it's not easy, even in America, where most men are circumcised at birth.

Now that three clinical trials in Africa have shown that circumcision helps protect men against AIDS and the World Health Organization has endorsed it, public health doctors elsewhere - including in New York City - are contemplating whether to recommend it. Then comes the difficult part - how to sell the idea.

Unfortunately, the data from Africa does not translate well. Those trials were of heterosexual men in countries where the virus is everywhere, education about safe sex is practically nonexistent, and condoms get in the way of the need to father children. In the United States, the AIDS epidemic is very different. The highest risk groups are men having sex with men (whether openly or covertly or even forcibly - in prison rapes, for example), people who share needles and women who, often unknowingly, have sex with high-risk men. Although it has been killing people here for 25 years, AIDS has not turned into a generalized epidemic like it has in Africa. Sex education, condoms, abstinence, antiretroviral drugs and the fear of death have concentrated it mostly in small pockets of the population.

And for most of those people, circumcision probably won't do much good. It might help protect gay men who are exclusively "tops" - that is, they have only penetrative anal sex, never receptive. It presumably would protect men having sex with infected women. It might protect women who choose circumcised men - but even that wasn't proved in the African studies, which had to be stopped early because the benefit for men was so glaring.

Because of these unknowables, no domestic medical authority, from the New York City Health Department to the American Urological Association, has a policy on adult circumcision yet.

And, besides, there hasn't been a groundswell of demand. "We haven't gotten a lot of calls," said Noel Alicea, a spokesman for Gay Men's Health Crisis, which runs a hotline. "Not a one," said Tokes Osubu, executive director of Gay Men of African Descent. "A few," said Mark McLaurin, executive director of the New York State Black Gay Network. "The first ones wanted to make sure that it wasn't going to be mandatory. And then there were others who said 'Tell me more - how much does this reduce my risk?'"

Mr. McLaurin said he would advise most gay men to "hold off until we have more data." But, he added, "for someone who was predominantly or exclusively a top, and said he was really having a hard time reducing his risk by practicing safe sex - I'd have a hard time recommending against it." But, he quickly added, he was certain that few men in his network would want it. "We've had a hard time recruiting black and Latino men even for vaccine trials," he said. "Because of everything from Tuskegee on up," he explained - referring to the notorious medical experiment in which black men with syphilis were left untreated for decades - many black Americans mistrust the medical establishment.

In Africa, it is relatively easy to talk men into getting circumcised, said Daniel Halperin, an AIDS researcher at the Harvard School of Public Health who has interviewed hundreds of African men about sex, AIDS and local customs. Some tribes circumcise teenagers to welcome them to full manhood. Many men who can't get enough water to bathe regularly think foreskins are unhygienic. And some, he said, "say circumcised men get all the women" because of a widespread belief that, with slightly lessened sensation, they can make love longer.

(Circumcision's effect on sex is a white-hot issue in the United States for the small but vocal antircumcision lobby. The lobby's main focus is on advice to parents of baby boys, but it has offshoot groups, like the "uncuts" who insist that sex with uncircumcised men is superior, and the "foreskin restoration movement" which utilizes tape, small weights and parental resentment.)

For adult men, circumcision takes about 30 minutes, said Dr. Craig Niederberger, chief of male reproductive surgery at the University of Illinois at Chicago. It is an outpatient procedure and, like dental work, can be done with local injections of Novocain. "But with many men," he added, "if you use the words 'scalpel' and 'penis' in the same sentence, they say 'put me to sleep!' So then we do it under general anesthesia." There is no official national estimate of how many adults have the operation each year.

Most of his patients have phimosis or balanitis - a painfully tight foreskin or swollen glans, which can become a crisis if urination is blocked. But, because he practices in a black Chicago neighborhood, some of his young, healthy patients are volunteers - perhaps the only demographic group of African-American men currently lining up for the operation. They are converts to Islam, which requires circumcision. "They come in very committed," he said. "It's a personal choice that's very strong." A spokeswoman for the Nation of Islam, the Black Muslim group also based in south Chicago, said she presumed most adherents were circumcised at birth, "but I'm the wrong person to ask," she added. A male official she suggested for comment did not return a phone call.

In any case, that appears to be the answer: Until more trials are done, it's going to take a medical emergency. Or divine intervention.

## 7. PHARMACEUTICAL INDUSTRY

### "Polymeric pain relief product to hit the shelves"

**Date:** 16 April 2007

**Source:** *in-Pharma Technologist.com*

**Author(s):** Anna Lewcock

<http://in-pharmatechnologist.com/news/ng.asp?id=75772>

US firm Skinvisible last week announced that its polymer-based delivery system has been licensed to pain relief company DRJ for use in a new topical analgesic product. DRJ will be using the delivery system to extend its range of 'Stopain' products with a new cream formulation incorporating Skinvisible's Invisicare delivery technology. Adding Invisicare to the product will significantly extend the period of time the product stays on the skin, stretching to four hours or more, allowing prolonged on-going relief for patients suffering from muscle-stiffness, arthritis or muscle strains.

The Invisicare group of polymeric delivery vehicles combine hydrophilic and hydrophobic polymers into stable complexes in water emulsions. The formula is designed for water-based creams and lotions to carry water-insoluble active ingredients without the use of alcohol, silicones, waxes or other organic solvents. The resulting product bonds active ingredients to the skin and is resistant to wash-off, delivering targeted levels of therapeutic agents directly onto the skin. The Invisicare range is available in a number of formulations of synthetic and natural polymers, with different specifications to meet the requirements of specific active ingredients. Products can be formulated as creams, lotions or sprays.

When applied to the skin, products formulated using the Invisicare polymers adhere to the skin's outer layers forming a long-lasting protective bond. According to Skinvisible, the product can allow enhanced delivery performance with improved efficacy, longer duration of action and require a lower dose of active ingredient. The sustained release also has implications for patient compliance, by allowing fewer applications with lower frequency without compromising therapeutic efficacy.

DRJ will be using the Invisicare technology to expand its offerings in its Stopain range of over-the-counter (OTC) topical pain relievers, further strengthening its position in the \$250m (Euros185m) topical analgesic market. "By including Invisicare, we are offering our customers a product that is different from anything else currently on the market," said Robert Miller, CEO of DRJ. "We expect this advantage to be well received by both the trade and the customer."

Skinvisible received its second US patent for the Invisicare polymer delivery technology in January 2006, covering the composition of the Invisicare delivery system. The company had already been granted a patent relating to manufacturing method, and has a third patent covering 'Methods of Use' currently pending.

The company's business model focuses on licensing its technology and proprietary Invisicare formulations to manufacturers of prescription and OTC products in the pharmaceutical and cosmeceutical industries.

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## 8. ANNOUNCEMENTS

### **New Document: Ethical challenges in study design and informed consent for health research in resource-poor settings**

[http://www.who.int/tdr/publications/publications/seb\\_topic5.htm](http://www.who.int/tdr/publications/publications/seb_topic5.htm)

This World Health Organization review considers ethical challenges to research design and informed consent in biomedical and behavioural studies conducted in resource-poor settings. A review of the literature explores relevant social, cultural, and ethical issues in the conduct of biomedical and social health research in developing countries. Ten case vignettes illustrate ethical challenges that arise in international research with culturally diverse populations.

Professional and public debates concerning the application of guidelines for ethical conduct in studies carried out in developing countries are likely to continue as new information becomes available. Researchers in biomedicine, public health, and the social and behavioural sciences confront the challenging task of adhering to national and international regulations in social and cultural environments in which ethical guidelines may not be easily translated or applied. Increased awareness of ethical concerns associated with study design and informed consent among researchers working in resource-poor settings is needed. But strengthening professional knowledge about international research ethics is not enough. Investigators also require practical advice on the best methods or models for articulating ethical guidelines in the field. Empirical research on a wide range of issues relevant to the application of ethical guidelines is needed, including studies of macro social and economic developments that drive the globalization of the biomedical research enterprise. Technological and financial resources are also necessary to build capacity for local collaborators and communities to ensure that results of research are integrated into existing health systems. This requires collaborative efforts and engaged commitment on the part of investigators, funding agencies, policy-makers, governmental institutions, and industry.

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