



# ALLIANCE FOR MICROBICIDE DEVELOPMENT

**07 December 2007, Volume 8, Number 47**

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](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. CORRECTIONS

### Finding the right product to fight AIDS

Last week's *Digest* featured the article "Finding the right product to fight AIDS." There is a correction to the author's name, which correctly should be written as Stephane Verguet. The Daily Californian has also updated their website (<http://www.dailycal.org/sharticle.php?id=27000>) with the correction.

### Trialists say they are not guinea pigs and wanted to take part

The Population Council has reached out to one of the reporters who penned the article titled "Trialists say they are not guinea pigs and wanted to take part," which ran in Health e-News and STAR newspaper on November 29, 2007.

They made some clarifications including:

- More than 6,000 women participated in the Phase 3 trial of the candidate **microbicide** Carraguard, which was conducted at three sites in South Africa.
- The participants were counseled that they could apply the gel within (or up to) an hour before sex. This means it can be used immediately before sex, with no wait, or up to an hour before sex.
- The average age of all the participants in the trial was under 30.
- The researchers do not know the status of the participants' partners.
- The trial started in March 2004. Preparations for the trial started in 2002. Participants stopped using and returned the gel to the study sites in March 2007, when data collection was completed. The trial data was locked in June, and the Population Council has been analyzing the data since that time.

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## 2. MONTHLY MICROBICIDE PIPELINE UPDATE

December 2007

<http://www.microbicide.org/microbicideinfo/reference/Microbicide.Ongoing.Clinical.Trials.Summary07Dec07.pdf>

Each month, the *Digest* includes an update on overall progress in the field. Currently, there are 11 **microbicide** candidates in clinical development and over 37 confirmed products in preclinical development. As a continued effort to maintain the most up-to-date information, we urge you to visit the Alliance website at [www.microbicide.org](http://www.microbicide.org) or contact Stephanie Tillman, Alliance Writer/Research Associate, by email ([stillman@microbicide.org](mailto:stillman@microbicide.org)) or by phone (301-587-3302) with any updates, questions, or comments.

*Please note: In the PDF version of the Digest, this table's formatting may render the entries difficult to interpret. For the correctly formatted version, please visit the web version of the Digest, or view the table on the Alliance's homepage, at [www.microbicide.org](http://www.microbicide.org).*

**MICROBICIDE CANDIDATES IN ONGOING CLINICAL TRIALS: SUMMARY AS OF DECEMBER 2007 \***

<i>Phase</i>	<i>Candidate Name and Formulation</i>	<i>Mechanism of Action</i>	<i>Sites by Country</i>
3	Carraguard (R) gel	Entry-fusion inhibitor	South Africa
3	0.5% and 2% PRO 2000/5 gels	Entry-fusion inhibitor	South Africa, Tanzania, Uganda, Zambia
2B	1% Tenofovir gel ("CAPRISA 004")	Replication inhibitor	South Africa
2-2B	0.5% PRO 2000/5 gel (P) and BufferGel (R) ("HPTN 035")	Entry-fusion inhibitor and Vaginal defense enhancer	Malawi, South Africa, United States, Zambia, Zimbabwe
2	1% Tenofovir/PMPA gel	Replication inhibitor	India, United States
1-2	Dapivirine (TMC120) vaginal ring	Replication inhibitor	Belgium
1-2	Dapivirine (TMC120) gel	Replication inhibitor	Rwanda, South Africa, Tanzania
1-2	Invisible Condom (TM) gel	Entry-fusion inhibitor	Cameroon
1	Dapivirine (TMC120) vaginal ring	Replication inhibitor	Belgium
1	Dapivirine (TMC120) gel	Replication inhibitor	South Africa

1	1% Tenofovir/PMPA gel	Replication inhibitor	Dominican Republic, United States
1	0.1% UC-781 gel	Replication inhibitor	United States
1	0.1% and 0.25% UC-781 gel <sup>Ã,Â±</sup>	Replication inhibitor	United States
1	0.1% and 0.25% UC-781 gel	Replication inhibitor	Thailand
1	3% VivaGel (TM) (SPL7013 gel)	Entry-fusion inhibitor	Puerto Rico, United States
1	3% VivaGel (TM) (SPL7013 gel)	Entry-fusion inhibitor	Kenya, United States
N-A	Vaginal ring safety and acceptability study	Placebo ring <sup>Ã,Â§</sup>	Kenya, South Africa, Tanzania

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For modifications, please contact Stephanie Tillman, email [stillman@microbicide.org](mailto:stillman@microbicide.org).

\*AMD is in the process of modifying its reports on clinical trials of **microbicides** in all relevant formulations.

<sup>Ã,Â±</sup> These trials have been completed and analysis of the final results is underway.

<sup>Ã,Â±</sup> This trial is testing the safety of the UC-781 vaginal **microbicide** applied rectally in men and women.

<sup>Ã,Â§</sup> This device is intended for use with a **microbicide**.

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### 3. MEDIA COVERAGE OF MICROBICIDES

#### "Gates Foundation gives group \$28.5M for microbicide research, officials say"

**Date:** 04 December 2007

**Source:** Kaiser Daily HIV/AIDS Report

[http://www.kaisernetwork.org/daily\\_reports/rep\\_index.cfm?DR\\_ID=49188](http://www.kaisernetwork.org/daily_reports/rep_index.cfm?DR_ID=49188)

The Eastern Virginia Medical School in Norfolk, Va., on Friday announced that its Arlington, Va.-based CONRAD program has received a five-year, \$28.5 million grant from the Bill and Melinda Gates Foundation to conduct **microbicide** research, the Newport News Daily Press reports (Flores, Newport News Daily Press, 12/1).

**Microbicides** include a range of products -- such as gels, films and sponges -- that could help prevent the sexual transmission of HIV and other infections (Kaiser Daily HIV/AIDS Report, 2/20).

According to Gustavo Doncel, director of preclinical research for CONRAD, the grant will fund research on a new generation of **microbicides** that use antiretroviral drugs. Antiretrovirals when taken orally have been effective in treating HIV, but this research will test their efficacy when used in a topical **vaginal gel** that could prevent the sexual transmission of the virus, the Virginian-Pilot reports. CONRAD Executive Director Henry Gabelnick said that the development of a **microbicide** is important because women are especially vulnerable to HIV transmission through

sexual activity. "It's clear that women are the majority of the new cases of HIV-positive people," Gabelnick said, adding, "If their partners won't use condoms, this gives women a product that they can use to protect themselves."

There are currently no **microbicides** on the market, but some have made it into the later stages of clinical trials, the Pilot reports. "The virus is much sneakier and cheekier than what we thought it would be," Doncel said. CONRAD is "poised to deliver something that is significant in the area of HIV prevention," Doncel added (Young, Virginian-Pilot, 12/1). The Gates Foundation to date has donated \$65 million to CONRAD for **microbicide** research (Newport News Daily Press, 12/1).

## "Behaviour change sure way to guard against HIV"

**Date:** 01 December 2007

**Source:** *Health-e*

**Author(s):** Khopotso Bodibe

[http://www.health-e.org.za/news/article\\_audio.php?uid=20031833](http://www.health-e.org.za/news/article_audio.php?uid=20031833)

The focus of this year's World AIDS Day is on leadership, with the slogans "Take the lead. Stop AIDS. Keep the promise". And a key emphasis is on how individuals can lead the response against AIDS.

KHOPOTSO: The only certain way to reduce HIV infection rates is through prevention. But no HIV vaccine is showing promise. Research into **vaginal gels** called **microbicides**, have also not found a protective get yet, although results of the Carraguard **microbicide** will be announced next month. But even if Carraguard works to protect women against HIV, researchers say it won't offer full protection. Studies into male medical circumcision have shown that it can reduce chances of men acquiring HIV from women by up to 60%. But without the use of condoms - the only proven protective measure available to us at the moment - that could spell danger. So, how best can we protect ourselves against HIV?

PREMIER MBHAZIMA SHILOWA: If we're going to really turn the tide, one of the things we've got to do is to look at what are we going to do to ensure that all of us change our behaviour. We decide individually - I'm aware and I intend to change my behaviour. It means if you're negative, you will try and ensure that you stay negative; that if you're positive, you will try and ensure that you don't infect someone else; that if you're positive, you will try and ensure that you do nothing that will ensure re-infection.

KHOPOTSO: Gauteng Premier Mbhazima Shilowa, speaking recently at the provincial government's AIDS conference. He said it's important for people to examine some of their behaviours and how they influence their actions.

PREMIER MBHAZIMA SHILOWA: Behaviour change also includes, by the way, our own lifestyles. Some of us go out, really drink beyond what we should do, we take drugs, and thereafter, we are happy, we are amorous, we are friendly, we're now more than generous with ourselves - and I'm talking both men and women... We need to be able to understand that it is those kinds of things that we need to think about.

KHOPOTSO: Put another way, says Shilowa, behaviour change is the power that many people have to individually safeguard against HIV infection, but fail to use.

PREMIER MBHAZIMA SHILOWA: What is important is to keep remembering that the decisions we take as individuals will ultimately determine whether we achieve the goal of an HIV-free generation. When all the information has been provided it is an individual's decision not to have sex, to be loyal to one partner or to use a condom. These are decisions that each and every one of us has to make. Sure, there is peer pressure... but in the end it's your decision.

KHOPOTSO: With efforts from the scientific arena to develop interventions to prevent HIV infections drawing a blank, scientists and researchers also agree that behaviour change is probably the best form of prevention available to stop increasing HIV rates. Professor Lynn Morris of the National Institute for Communicable Diseases, in Johannesburg, is heavily involved in HIV vaccines research in South Africa. Recently, a study called Phambili had to be abandoned after interim results from a sister trial in the United States showed that the vaccine does not offer any protection.

Prof. LYNN MORRIS: As you know many of the preventative things that we're trying - the **microbicides** are not proving very effective, obviously, this vaccine trial is extremely disappointing, the diaphragm study showed no effect - so, really, from a public health point of view we're finding it very difficult, actually, to intervene and stop the spread of this virus. Of course, there are other ways that people can protect themselves - obviously, behaviour change and condoms - and that's what we've got to really press home to people, that they need to be adopting those kinds of practices because, I think, it's going to be a long time before we have a vaccine.

KHOPOTSO: On the **microbicide** research front, results of the only product to have completed all research processes are expected early next year. Dr Khatidja Ahmed is the Principal Investigator in the Carraguard trial.

Dr KHATIDJA AHMED: We're looking at prevention being better than cure. So, a lot of emphasis has been placed on prevention methods, as you correctly say. We have behavioural changes, which, of course, is the most important part of it all.

KHOPOTSO: Condoms are the only method to prevent HIV infection for those who are sexually active. But they have to be used consistently and with care. They form part of the universal ABC strategy of prevention, which focuses on behavioural change. But behavioural change goes much further than simply abstaining from sex, being faithful to one partner and using condoms. Some would also argue that the ABC strategy is too simplistic for certain groups of society, such as women who cannot always negotiate safe sex. Perhaps it's time for a national dialogue on behavioural changes and HIV prevention, just like there has been on AIDS treatment.

## "Leadership vital in war on AIDS"

**Date:** 01 December 2007

**Source:** *The Star (Toronto)*

**Author(s):** Editorial

<http://www.thestar.com/comment/article/281512>

Each year, one day is set aside as a reminder to the world that millions of people are still dying from a disease that was discovered decades ago and for which there is no cure, no vaccine and which the richest countries, like Canada, have done far too little to combat.

That day is today, World AIDS Day 2007.

New figures released last week by UNAIDS, the United Nations agency charged with dealing with HIV/AIDS, illustrate the devastating toll of this dreadful disease, with an estimated 33.2 million people worldwide infected with HIV. This year alone, 2.5 million people became newly infected with HIV and 2.1 million died of AIDS. Almost two-thirds of the overall deaths have occurred in sub-Saharan Africa, leaving the region to cope with growing numbers of AIDS orphans.

But there is a glimmer of hope in the grim statistics. UNAIDS now says there are 7 million fewer people infected by HIV than it had previously estimated. And some scientists now believe the epidemic may have passed its peak.

While much has been done in recent years, agencies working to find a cure for HIV and AIDS and that deal with treating patients already stricken with the disease are constantly short of money and other resources. For example, women now make up 14 million, or 61 per cent, of HIV infections in Africa, yet a proposal for a new UN agency that would focus specifically on women and HIV/AIDS sits in limbo.

At the same time, more money is needed to develop a vaccine and **microbicides**, creams that prevent HIV transmission during sexual contact. Promising trials for both failed this year, a setback for development. More funds are also needed for drugs and a variety of education and prevention programs, including male circumcision, which recent studies have found greatly reduce the risk of getting AIDS.

Prime Minister Stephen Harper's efforts on the AIDS front have been scattered at best. Although he cancelled a funding announcement at the World AIDS Conference in Toronto in August 2006, he did pledge \$120 million last December to the AIDS battle.

In February, he announced Canada would contribute up to \$111 million in new funds toward a Canadian HIV Vaccine Initiative, partly to set up a new facility to manufacture and test vaccines. The initiative is partly funded by the Bill and Melinda Gates Foundation, which contributed \$28 million. But published reports this week suggest some of Ottawa's money may have been taken from community AIDS prevention programs in Ontario, which have seen funding cut 30 per cent.

And earlier this week in Tanzania, Harper tried to gain widespread publicity by announcing his government would spend \$105 million over five years to help save children in Africa and Asia from tuberculosis, malaria and AIDS. What Harper failed to mention was that the government had previously announced the funding.

What should Harper do to help combat this disease?

First, he can speed passage of federal legislation that would allow makers of generic drugs to make cheap copies of expensive patent-protected medicines for AIDS-stricken countries. The legislation has been entwined in red tape for

years, with the result that not a single generic drug has yet made it to Africa.

Second, he can boost Ottawa's spending on AIDS. Last September, Canada was urged to commit \$900 million over three years to the Global Fund to fight AIDS, malaria and tuberculosis. To date, 25 other countries have stepped up. Ottawa has said nothing.

Third, Harper also can focus more attention on AIDS in Canada, where more than 62,000 people are living with HIV/AIDS. New infections are often among young people, especially girls 15 to 19 years old.

Harper should take note of the theme for this year's AIDS Day, which is leadership. Twenty-five years after the AIDS epidemic first erupted, that leadership is still badly needed.

### **"Overtaken by hype"**

**Date:** 01 December 2007

**Source:** *The Times of India*

**Author(s):** Editorial

[http://timesofindia.indiatimes.com/Opinion/Editorial/LEADER\\_ARTICLE\\_Overtaken\\_By\\_Hype/articleshow/2586571.cms](http://timesofindia.indiatimes.com/Opinion/Editorial/LEADER_ARTICLE_Overtaken_By_Hype/articleshow/2586571.cms)

In 1987, no one wanted to hear about AIDS. Twenty years later, the wheel has come full circle. The spokes, however, are completely different. When it first hit India, the reason was squeamishness, which was why the afflicted, health workers, sociologists and the media shied away from it. Today's resistance stems from weariness. It's a case of overkill.

Large sections of people have begun to manifest serious symptoms of AIDS fatigue. They are fed up of the celebrity circus jumping literally on to the bandwagon. Passive resignation has turned to articulate protest. They demand to know why only AIDS gets this hoopla when there are deadlier monsters on the prowl. Several afflictions, from diarrhoea to drunken driving, reportedly kill more people than the opportunistic infections which take over when HIV disables the host's immune system. Should more deserving illnesses be deprived of the right degree and right kind of attention simply because they aren't sexily global?

It's not an unjustified gripe. The India of the BRIC report also ranks on the international health register, but more dubiously. We occupy pole position in several diseases. Our rate of preventable blindness is as unstoppable as that of our economic growth. We have had less success with containing diabetes than with containing inflation. As for our showpiece, the conquest of polio, swallow this: India accounted for over half the world's 720 cases in the current year, dislodging the earlier top ranker, Nigeria. Globalisation has not only pumped up our GDP; consumerist lifestyles have increased hypertension and obesity. Schools have to contend with growing attention deficit disorders, even suicides. Hepatitis has long been endemic to our arrogant cities, to which add leptospirosis. Are these killers too downmarket for our designer Bleeding Hearts? Why haven't they jumped aboard with fund-raisers and photo-ops?

There is another kind of déjà vu in the public's reaction to AIDS. Now, as way back then, it is being condemned as a

'Western' blot. In the early years, it was smugly dismissed as a problem of debauched America/Europe. Now, there is a suspicion that the West is pouring in the funds and keeping up the attention not out of a noble concern for Africa and Asia, but out of narrow self-interest. It is afraid that our AIDS could easily be exported - or repatriated - through today's porous borders. These arguments may seem unduly cynical, even ungrateful, but they are there.

So this AIDS Day, who will be heard louder, the usual pros or those who think it's a con? The bets are still on the AIDS lobby which is undeterred by either the good news or the bad news. The good news is that, thanks to more accurate reporting methods, the estimates of AIDS prevalence in India have been slashed; the current figure is 2.5 million. The bad news is that 28 years after it was identified in the US, we have not succeeded in finding either cure or prevention. All we still have is the primitive condom or the iffier 'No'.

Treatment may have improved from the ravaging AZT to a more benign cocktail of ARVs, but resistance has grown to first-line drugs, and everything is fiendishly expensive and accessible only via heavily subsidised NACO programmes. This again triggers the 'what-about-us' protest from other health lobbies fighting for a slice of an unfortunately small pie.

Preventive technologies have not struck pay-dirt either despite the promises and the expense of research and clinical trials. Both vaccines and **microbicides** have run into one controversy after another; the STEP trials for the Merck vaccine were called off in September, and those for cellulose sulphate last January. So, ask the antagonists, why are we wasting precious money only on this disease instead of the easier-to-tackle malaria or maternal mortality?

There is a long answer on how AIDS is not just a health issue, how it extracts a serious social and economic price for generations, and how all stigmatised diseases need the extra oomph. The short answer is that damning AIDS advocacy will not necessarily divert the flow to other health issues. Such serious concerns can never be either/or. Better, instead, to deploy the classical strategy of 'If you can't beat them, join them'. Or, more aptly, imitate them. The Hindi proverb, 'Only the crying baby gets the milk', applies when resources are limited. There is much to learn from the advocacy efforts of the AIDS warriors.

More important, just as fitness has acquired a stronger cachet than illness, prevention should be the cornerstone of all lobbying efforts for all diseases. The search for a vaccine was first off the mark when AIDS struck North America in 1980, but it was elbowed aside by a traumatised community demanding the immediate solution of a cure. Precious years were lost, but impressive work on preventive technologies has been done in the last few years, catalysed by such global groups such as Dr Seth Berkley's International AIDS Vaccine Initiative and Dr Zeda Rosenberg's International Partnership for **Microbicides**.

The 'why only AIDS' lobby should have no quarrel with their approach which encompasses advocacy, R and D and ethical trials. The funds are globally sourced, India will be a major beneficiary, and AIDS prevention will take the pressure off not just expensively subsidised lifelong treatment regimens, but the whole overburdened health-care system. Both gains will free up resources for less hyped and more prevalent ailments.

## "Vigilance and setbacks in the AIDS fight"

**Date:** 01 December 2007

**Source:** *The Boston Globe*

**Author(s):** Max Essex, Loretta McLaughlin

[http://www.boston.com/bostonglobe/editorial\\_opinion/oped/articles/2007/12/01/vigilance\\_and\\_setbacks\\_in\\_the\\_aids\\_fight/](http://www.boston.com/bostonglobe/editorial_opinion/oped/articles/2007/12/01/vigilance_and_setbacks_in_the_aids_fight/)

Seldom has the prospect of containing the AIDS epidemic looked so discouraging. The best strategies for preventing the spread of the disease have always been the creation of a preventive vaccine or a gel able to kill the AIDS virus when applied before sexual intercourse.

These measures are far more reliable than the important but limited public health practices currently available - trying to change human behavior in terms of condom-protected sexual pursuits and/or abstinence, or trying to prevent exposure to contaminated blood via needles used by drug abusers.

As matters stand, the extraordinarily wily HIV virus, which causes AIDS, infects more than 33 million people worldwide, according to the United Nations.

Nearly a quarter-century ago, Margaret Heckler, the secretary of Health and Human Services, predicted a vaccine against AIDS would be ready for testing within two years. Now most AIDS specialists predict that it will take at least 20 years before we have one that works.

In September, human trials using the most promising anti-HIV vaccine, the Merck model, were stopped. And for good reason. Hopes had been high that this vaccine might largely, if not wholly, prevent the transmission of new HIV infections. Ideally, such a vaccine would also help as a treatment for patients already infected by lowering the quantity of internal virus production.

The vaccine used a common cold virus (adenovirus 5), weakened so as not to cause any respiratory illness, as a vector for the HIV components. Attached to this respiratory virus were harmless segments (three key genes) of HIV known to be ones that would prompt the immune system to single them out as the targets of a full-scale attack against them. It was reasoned that the immune system would produce enough anti-HIV responses to protect a person against exposure to HIV. The Merck model vaccine had worked that way in monkeys, but it didn't work in humans.

Not only was the HIV-specific immune response insufficient to protect people, there were also worrisome suggestions that the vaccine might enhance the likelihood of HIV infection following exposure in real life.

No one is certain how this vaccine might inadvertently increase the risk of HIV infection. Some specialists speculate that since most of us carry biologic "memories" of adenovirus 5, its use as a vector for HIV genes might have inadvertently stimulated an outpouring of the wrong immune response cells, some of which were then more susceptible to real HIV shortly after vaccination.

Cancellation of the Merck vaccine trials was particularly disheartening within the AIDS research community because it

will hold up trials with the next promising vaccine in line for testing, a model from the National Institutes of Health model that somewhat resembles Merck's.

This was not the first AIDS vaccine to fall by the wayside. Earlier this decade, others had failed whose designs were more closely patterned after the prevailing vaccines against such diseases as polio and measles. The Merck vaccine design was revolutionary by comparison.

Other promising anti-AIDS agents also have failed in human trials. **Microbicides** - gels to thwart the AIDS virus by harming or killing it - were first seen some 10 years ago as likely candidates to prevent the spread of AIDS on a large scale.

Results from trials with the first HIV **microbicide**, nonoxynol 9, were reported five years ago. This year, results from the second such product, Ushercell, came in. Both not only failed to protect against HIV transmission during sexual intercourse, but also seemed to increase the risk for HIV infection.

Fortunately, progress with drugs to treat and control AIDS disease has been substantial. Through combinations of these medicines, the majority of patients in such economically advantaged nations as the United States live out extended and productive lives. For them, AIDS is no longer the death sentence it once was.

Such success with anti-AIDS drugs, however, is still more the exception than the norm across the world. Only 10 percent of the tens of millions living with HIV today have access to effective drugs. Through long-term, multibillion-dollar programs like President Bush's Emergency Plan for AIDS Relief, the Global Fund, and the Clinton and the Bill and Melinda Gates foundations, millions more AIDS patients in developing countries will receive treatment next year and beyond.

Today, more is known about the AIDS virus than any other in medical history, even though it changes its structure billions of times in each infected person - far more than any other virus.

Still, AIDS has become the leading cause of death in all of southern Africa and in many populations of young adults worldwide. While success with treatment is now reality, prevention of AIDS through vaccines and **microbicides** will follow as long as we remain committed.

### "Highlights of biomedical prevention strategies"

**Date:** 30 November 2007

**Source:** *The Body*

**Author(s):** Keith R Green

<http://www.thebody.com/content/art44127.html?mtrk=4304073>

A significant portion of this year's International AIDS Society Conference was devoted to current developments in the area of HIV prevention -- specifically, those that have come to be known as biomedical prevention. Unlike traditional

prevention strategies, such as the promotion of condom use and the knowledge of one's own HIV status, biomedical prevention generally involves strategies that are more deeply rooted in medical science, requiring more rigorous and heavily scrutinized study in clinical trials before they are approved for use among the general population.

In addition to discussion about recent trials involving HIV vaccine candidates (the original attempt at biomedical prevention, which have been slow coming and often disappointing in their development), the IAS Conference this year focused on four other emerging and innovative technologies that are gaining momentum around the world -- pre-exposure prophylaxis (PrEP), male circumcision, **microbicides**, and HSV-2 (herpes simplex virus type-2) suppression.

### *PrEP*

Clinical trials that are currently exploring the safety and efficacy of PrEP involve the use of currently approved anti-HIV medications -- Viread (tenofovir) in particular. In these studies, antiretrovirals are prescribed to high-risk HIV-negative people in an effort to prevent the onset of the virus in the event of actual exposure.

Trials are presently underway in several countries, including Thailand, Botswana, Peru, Ecuador, and the United States, most of which are safety trials. The study in Thailand, which is specifically looking at the use of PrEP in intravenous drug users, appears to be furthest along, with preliminary data projected to be available in the spring of next year and a final analysis expected the following year. There is also a safety trial being developed in that country which explores the use of Viread as an alternative prevention strategy for women.

The trial in Botswana is looking at both heterosexual men and women, while trials in Peru and Ecuador are exploring the use of PrEP in men who have sex with men (MSM).

Researchers are very optimistic about these trials for a number of reasons. "Number one," explains Dawn Smith, M.D., MS, MPH, a principle investigator for PrEP clinical trials conducted through the U.S. Centers for Disease Control and Prevention (CDC), "is that there is biological plausibility.

"We know that these drugs have concentrated levels in the genital tract, which is where the majority of the world's transmission occurs. We know that it works in animal models. We know that PrEP works for post-exposure prophylaxis [after exposure to the virus]. And we know that safety was demonstrated in the FHI [Family Health International] trial that has already been completed."

Smith stressed the importance of preparing for the implementation of PrEP even before trial results are in because, she says, we've never had a biomedical prevention method such as this one in the U.S. Therefore, she explains, the CDC will need adequate time to prepare for it. And even if by some small chance these trials prove to be ineffective, this planning will still be useful for "the next biomedical intervention, whether that be **microbicides** or vaccines," she said. "So it's not a wasted exercise in that event."

Smith argues that the most important advantage to PrEP, aside from the fact that it may work for more than one type of exposure, is that it is the first opportunity to get high risk people in for periodic risk reduction counseling and HIV

testing.

### **Microbicides**

Hope for an effective prevention method that women, in particular, can control was dampened at the conference when news regarding the failure of a once promising **microbicide** was presented. Data from two studies showed that UsherCell, a **microbicide** containing 6% cellulose sulphate, did not protect women against sexually transmitted HIV infection, and suggested that it may have even contributed to an increased risk of HIV acquisition.

**Microbicides** are anti-HIV substances, in the form of creams or gels, that can be applied to the vaginal or rectal areas in an effort to prevent HIV infection. There are currently no **microbicides** approved for use, however, there are a number of them being studied in clinical trials.

UsherCell showed no signs of potential harm in pre-clinical testing, and was considered to be acceptable to the women in the studies, causing minimal side effects when used vaginally.

A large-scale phase 3 study of the **microbicide** that was being conducted in Benin, South Africa, Uganda, and India was stopped in January 2007, however, when an interim analysis revealed that more women who were actually using the gel had become infected than those using a placebo gel. These findings also led to the pre-mature termination of UsherCell trials in Nigeria, though upon analysis of these studies, the women enrolled in this country were experiencing an opposite effect (which researchers did not deem statistically significant).

Scientists are still uncertain as to what may have been the cause of these disappointing findings, but speculate that there may have been inflammatory reactions to the gel, and/or localized immune dysfunction or disruption of the normal vaginal flora as a result of frequent cellulose sulfate use. Extensive testing is currently being done to accurately determine the cause of failure.

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

### **"The search continues for female-controlled HIV prevention methods"**

**Date:** 30 November 2007

**Source:** *National Womens Health Network*

**Author(s):** Julia Matthews

[http://www.nwhn.org/wha\\_novdec07\\_ibiscbas?layout=print&PHPSESSID=51f9b9603436bd508c4b2da0fbe77178](http://www.nwhn.org/wha_novdec07_ibiscbas?layout=print&PHPSESSID=51f9b9603436bd508c4b2da0fbe77178)

The number of women infected with HIV rises each year across the globe. In the United States today, women account for more than one quarter of all HIV/AIDS diagnoses and AIDS is the leading cause of death among black women

ages 25--34 years.<sup>1</sup> In sub-Saharan Africa, close to two-thirds of people living with HIV in 2006 were women.<sup>2</sup> In fact, for every 10 adult men infected with HIV in this region, there are approximately 14 adult women who are HIV-positive.<sup>3</sup>

Women and girls are at high risk for HIV infection due to a number of factors, including biologic vulnerability, economic dependence, and a lack of power in their relationships. Because men do not always agree to use condoms, there is an urgent need for HIV prevention methods that women can control. (See the May/June issue of the WHA for an overview of **microbicides**' role in HIV/AIDS prevention.) One idea currently being explored is using the diaphragm to prevent disease transmission. Because the cervix is both more vulnerable to infection than are other parts of the vaginal tract, and home to many cells that can be infected by HIV, researchers recently conducted a study to determine whether covering the cervix with a diaphragm during sex reduces a woman's HIV risk.

The Methods for Improving Reproductive Health in Africa (MIRA) trial, led by researchers at the University of California, San Francisco, was a randomized, controlled trial that measured the effectiveness of the diaphragm and lubricant gel in preventing HIV infection among women. More than 5,000 sexually active women from South Africa and Zimbabwe participated in the study; these women received voluntary counseling and testing, safer-sex counseling, free male condoms, and diagnosis and treatment of sexually transmitted infections. Half of these participants (the intervention group) were randomly selected to receive, in addition, a latex diaphragm and Replens gel, which is a non-contraceptive lubricant.

Unfortunately, the MIRA results showed that there was no statistical difference in the rate of new HIV infections between women in the intervention group and those who only received male condoms to use as protection.<sup>4</sup> Therefore, the results do not support the addition of the diaphragm to current HIV prevention strategies for women. Although these results are disappointing, it is important that this research was done. The MIRA trial made a significant contribution to the HIV prevention field and the trial's important qualitative findings also will inform future research on female-controlled prevention methods.

Despite these findings, the MIRA team concluded that studies should continue to examine the potential of cervical barriers for HIV prevention. Future research may address validating participants' self-reported behaviors or assessing their adherence to study products (e.g., use of the diaphragm). Meanwhile, new kinds of cervical barriers are being developed such as the SILCS diaphragm, a one-size-fits-most diaphragm, and the BufferGel Duet, a combination **microbicide** and diaphragm-like device. The diaphragm may also be an ideal applicator for candidate **microbicides** (topical products that can reduce the risk of HIV and other sexually transmitted infections when inserted before sex), because it has a long history of safe use, has been approved by regulatory bodies around the world, and is reusable.

Currently, the female condom is the only existing female-initiated HIV prevention method, and merits greater investment and efforts to promote its use globally. Equally important is continued research on female-controlled prevention methods such as **microbicides** and an AIDS vaccine. Greater access to existing methods and the identification of new female-controlled HIV prevention methods are key steps to saving the lives of women and girls worldwide.

## "SA holds breath on HIV microbicide; scientists analyse results of four-year trial"

**Date:** 30 November 2007

**Source:** *Cape Argus (Cape Town)*

**Author(s):** Di Caelters

<http://www.capeargus.co.za/>

Local researchers, along with the HIV/Aids community worldwide, have two nail-biting months to go before they know whether a South African **microbicide** trial is a success. Testing of the product, which is entirely different from the one for which tests were halted after failed safety checks this year, has taken four years.

But the Phase 3 human trials are now complete, according to Sumen Govender, clinical studies director at the Population Council. The results were being analysed and were expected to be announced in February, he said.

**Microbicides**, effectively a gel that women insert before having sex to protect them from HIV infection, have been hailed internationally as a vital prevention method that is controlled by women. The product, Carraguard, carries with it a \$60-million research price tag that came courtesy of the Bill and Melinda Gates Foundation and the US Agency for International Development.

It was one of the Population Council's scientists, David Phillips, who started the Carraguard ball rolling in New York, home to the council's headquarters, Govender said. Alana de Kock, co-principal investigator at the Gugulethu trial site, said more than 6 200 South African women were involved in the four-year trial, about half from Cape Town and the remainder from Pretoria and Durban.

The trial was overseen jointly by the Infectious Diseases Epidemiology Unit at UCT's School of Public Health and Family Medicine, the SA Medical Research Council, and the Sechaba Research Centre. Women of 16 years and older who were HIV-negative were enrolled for, at the longest stretch, two years. Half were given a placebo and half the active gel, which is made and packaged in Sweden. The gel had to be used with condoms.

The **microbicide** trial that was halted for safety reasons at the end of January was to test a cellulose sulphate-based topical gel and included 1 500 women in South Africa, Benin, Uganda and India. Twenty South Africans were infected with HIV during the trial.

De Kock said strict checks and balances had been applied throughout to the Carraguard study here, and the trial's Data Monitoring and Safety Board had allowed it to run to its completion date in March.

The main ingredient in Carraguard is carrageenan, which comes from seaweed and has been used for hundreds of years. It is used in cosmetics and is an ingredient in such items as baby formula and toothpaste. Before the Phase 3 human trials, Carraguard first underwent laboratory testing, then Phase 1 trials which were done in all parts of the world, followed by Phase 2 trials in Gugulethu and Garankuwa.

Govender said the Population Council had two other potential **microbicides** in the pipeline. The first was an antiretroviral-based gel combined with a **microbicide** for which laboratory testing was now complete. The second was a combined **microbicide**-contraceptive and still in laboratory testing. Both studies were awaiting the Carraguard results before proceeding.

Govender said although the council was sourcing Carraguard from Sweden, it had the commitment that pharmaceutical companies in South Africa would come on board to manufacture the **microbicide**, should it become available.

"Sweden would transfer the technology to South Africa because we would be able to manufacture the product more cheaply," he said.

**EDITOR'S NOTE: A subscription is required to view this article at its original location.**

**"This war must be won!"**

**Date:** 30 November 2007

**Source:** *The San Diego Union-Tribune*

**Author(s):** Vishwas R Gaitonde

[http://www.signonsandiego.com/uniontrib/20071130/news\\_lz1e30gaitond.html](http://www.signonsandiego.com/uniontrib/20071130/news_lz1e30gaitond.html)

It is a military maxim that if the loss of a battle disheartens you, you are on your way to losing the war. Tomorrow (World AIDS Day), researchers, health officials, people infected with or affected by the human immunodeficiency virus will be ruminating on the battle just lost - the dramatic flop of the HIV vaccine, V520, developed by the U.S. pharmaceutical giant, Merck. Others developing similar vaccines have halted their trials, though some, developing dissimilar vaccines, are carrying on. Nevertheless, many researchers feel dejected, with good reason.

HIV is a moving target. Its propensity to mutate makes it a virtual new entity beyond the reach of the vaccine developed against its former self. V520 was believed to stand the best chance of the vaccines under development, but "dramatic flop" is not even the right term for the fiasco. Not only did the vaccine fail to protect the people who received it, but there were more infections among those who received the vaccine (49 out of 914) than those who received a placebo (33 out of 922).

The vaccine consisted of HIV genes loaded on to a modified common cold virus, which acted as a carrier vehicle. When introduced into a person, the piggybacked HIV genes were to trigger an immune response that would galvanize the CD8 lymphocytes. These cells, like a committed SWAT team on a mission, specifically seek out HIV-infected cells and destroy them. So while the vaccine may not have offered total protection, it would have minimized the effects of a future HIV invasion.

The vaccine itself is unlikely to have caused the new infections. But how it raised susceptibility to HIV in the recipients is not clear, though experts have proposed various theories. Were the HIV genes faulty? Was the common cold virus the wrong carrier? Were there any host factors at play? For instance, were participants also simultaneously infected by some other virus such as herpes or hepatitis C that could have acted as spoilers? Another interesting fact: Almost all the vaccinated volunteers who were subsequently infected with HIV were males, though females formed a sizable section of the study population.

So there are many questions to be answered - and they may well shed light that will help the development of future vaccines. And piggybacking HIV genes onto a carrier virus is just one way of stimulating the immune system; other

ways exist.

The United Nations has revised its estimates about the number of HIV-infected people in 2007 from 39.5 million to 33.2 million, largely because figures for infection in India were revised using a system of surveillance and data collection different from the one previously employed. But this is no more a cause for complacency than the failure of the Merck vaccine is grounds for hopelessness and dejection.

The 33.2 million will require treatment, some today, others tomorrow. Antiretroviral treatment is lifelong, and despite costs of medications coming down, it is still beyond the reach of many of the infected. Sub-Saharan Africa still has the maximum number of cases (22 million) but Asian countries show the fastest-growing rates of new infection, and the number of new cases since 1999 have nearly doubled in the European Union.

Critics point out that the majority of HIV-infected people do not know they harbor the virus because the early stages of the disease are symptom-free, so the total numbers could be higher than estimates obtained by any data-collection method. If the numbers of new infections continue to rise unchecked, then the hard-fought gains can slip away.

Also, the hype (clearly premature, in the light of current events) that new doodads - an AIDS vaccine, or a **microbicide** gel or cream that prevents sexual transmission - are around the corner can cause a false complacency and subsequent relaxation of the mainstay staples: preventive measures and antiretroviral treatment. This is like not effectively using your current military aircraft because you are eagerly awaiting the ultra-super stealth bomber that is being developed. In the meantime, the enemy makes covert inroads, stealthily gaining on you.

The disheartened must peek into history. It took several centuries to control, cure or eradicate the infectious diseases that mauled people since antiquity: the bubonic plague, smallpox, tuberculosis, leprosy, polio, rabies, cholera, typhoid. By contrast, AIDS was first detected and defined in 1981, and within a quarter-century, we have an array of drugs and sufficient knowledge about how its spread can be prevented.

Even the story of the polio vaccine is illuminating. The quest started in the early 1900s but kept failing. One reason was that the scientists did not know there were three serotypes of the poliovirus: PV1, PV2 and PV3. But the research continued painstakingly, funded by various sources from grass-roots organizations such as the March of Dimes Foundation right up to the president, Franklin D. Roosevelt, himself afflicted with polio.

Only in 1952 did Dr. Jonas Salk break through with a successful injection polio vaccine. A decade later, Dr. Albert Sabin introduced an oral polio vaccine. But the original Salk vaccine, successful in decimating the incidence of new polio infections, was defective in that some virus particles were not completely inactivated, and actually caused 260 new polio infections, including 10 deaths.

Those old enough to remember this must experience a sense of déjà vu when reading about the V520 HIV vaccine causing new HIV infections. But once the problem with the Salk vaccine was corrected, it became a pretty effective vaccine. The lesson, then, is that failure must be treated as a stepping stone to success.

**"Bug zapper: microbicides promoted to stop spread of HIV, other STDs"**

**Date:** 29 November 2007

**Source:** *Sacramento News and Review*

**Author(s):** Kel Munger

<http://www.newsreview.com/sacramento/Content?oid=602591>

According to World Health Organization estimates, somewhere between 5,000 and 7,000 women will be infected with HIV, the virus that causes AIDS, today.

Some of them will be infected because they couldn't convince their partners to wear a condom.

"I've done research with all kinds of women, from low-income women to law students, and condom negotiation is always a tough one," said Bethany Young Holt, an epidemiologist at UC Berkeley and director of the Sacramento-based California **Microbicide** Initiative. Holt's specialty, **microbicides**, may help those women protect themselves from infection no matter what decisions their partners make.

**Microbicides** are products - gels, lotions, solutions - that are applied topically to either the vagina or rectum before sex in order to stop the transmission of infectious microbes. That means everything from viruses like HIV to the bacterium that causes gonorrhea to the spirochete that causes syphilis.

Put bluntly, **microbicides** kill the microbes - micro-organisms, or less precisely, "bugs." Without the bugs, no disease.

"This is a new tool for prevention," Holt told SN and R. "**Microbicides** are not the magic bullet - they won't cure AIDS. Nothing probably will be a single magic bullet. But these will empower women to protect themselves from infection."

In California, 45 percent of HIV infections in women come from heterosexual contact, more than any other source, including intravenous drug use. But for a variety of reasons, women may not feel they can protect themselves from possible HIV transmission. Holt has done studies in communities as disparate as Ethiopia and Oakland, and she said that the problem is pretty much the same.

"In a lot of communities, if a woman is married and she's afraid that her husband is not safe, abstinence is not practical," Holt said. "There are also situations where a lot of abuse is involved, so the ability to protect herself is paramount." And that's just where **microbicides** offer hope. Rather than convincing a partner to put on a condom, women - and for that matter, men who are having sex with men - can use the **microbicide** to prevent themselves from becoming infected.

Holt said that there are currently about 30 **microbicides** under development, with a number that have progressed to clinical trials. "There are all sorts of compounds and formulations," she said. "Some are maintaining just normal vaginal flora" - that is, keeping the Ph of the vagina at its normal acidity so that HIV can't thrive in semen. These particular **microbicides** offer a useful side effect, depending on your perspective: They can stop the transmission of HIV, but don't affect conception. For women who wish to conceive without contracting or passing on HIV, **microbicides** like this would be, quite literally, life savers.

There are also products under development that function as both **microbicides** and spermicides, providing both protection from HIV transmission and contraception.

And in addition to preventing transmission of HIV, the **microbicides** can be effective against other sexually transmitted diseases, like Chlamydia, and infections such as bacterial vaginosis. "These infections are on the

pathways - they make you more vulnerable - to HIV infection," Holt said. "If we can be successful in developing **microbicides** for STDs and other infections like bacterial vaginosis, we can not only reduce these infections, but reduce the likelihood of HIV transmission."

Holt's organization, CAMI, is among many that have done studies of both the acceptability and cost-effectiveness of **microbicides**. According to Holt, "These studies show that the market for **microbicides** is there, and that they could save a lot of money in prevention, say, in preventing Chlamydia."

But most research is being done by small companies, including some nonprofits. And research takes money. Among the legislative hopes for **microbicide** research is the **Microbicide** Development Act, a federal bill aimed at directing HIV/AIDS prevention research funds for **microbicides** to the appropriate places. "The MDA isn't asking for more money for **microbicides**," Holt said. "It's saying that we have this money, so let's consolidate it for the best use." The MDA has been introduced a number of times in Congress but has yet to pass. "It's important to encourage California legislators to sign on for passage of the MDA," Holt said.

In the meantime, some **microbicides** are already in clinical trials, and a number of area health providers - including Planned Parenthood Mar Monte, Kaiser Permanente and UC Davis Medical Center - have signed on with CAMI to assist in the trials. "We need to be very ethical with these trials," said Holt. "While it's important to get **microbicides** that work, they need to be safe, as well as effective." She pointed out that both men and women will be using the **microbicides** in "very sensitive areas," so it's not enough to be effective; the products will need to be completely safe.

Katharyn McLearn, director of public affairs for Planned Parenthood Mar Monte, told SNandR that exploring new reproductive health advances is "core to our mission." Planned Parenthood "is currently in Phase II testing of a **microbicide**," she said. "The more options people have, the more likely they will be to find a method that works for them." McLearn also told SNandR that starting this month all local Planned Parenthood clinics are providing rapid HIV tests, which will provide results within 20 minutes at low cost - in some cases, free.

People who are interested in participating in a **microbicide** trial should contact CAMI through their Web site at [www.cami-health.com](http://www.cami-health.com).

According to Holt, California is the perfect place to do **microbicide** research. "This is such a promising tool, and California is such an economic and cultural leader," she said. "We should be able to step up and see that these things are developed safely."

## "Ten myths and one truth about generalised HIV epidemics"

**Author(s):** Shelton JD

**Reference:** N/A 370(9602):1809-1811. Comment.

<http://www.thelancet.com/journals/lancet/article/PIIS0140673607617553/fulltext>

**Published Abstract:** Despite substantial progress against AIDS worldwide, we are still losing ground. The number of new infections continues to dwarf the numbers who start antiretroviral therapy in developing countries.<sup>1,2</sup> Most infections occur in widespread or generalised epidemics in heterosexuals in just a few countries in southern and

eastern Africa. Although HIV incidence has fallen in Uganda, Kenya, and Zimbabwe, the generalised epidemic rages on. Something is not working. Ten misconceptions impede prevention.

*HIV spreads like wildfire* - Typically it does not. HIV is very infectious in the first weeks when virus levels are high,<sup>3</sup> but not in the subsequent many-year quiescent phase. Only about 8% of people whose primary heterosexual partners have the virus become infected each year.<sup>4</sup> Thus Kenya has more couples in which only one person is infected than couples in which both are (figure).<sup>5</sup> This low infectiousness in heterosexual relationships partly explains why HIV has spared most of the world's populations. However, the exceptional generalised epidemics in Africa seem largely driven by concurrent partnerships, in which some people have more than one regular partner. This pattern allows rapid dissemination when a new infection is introduced<sup>6</sup> and probably involves more frequent risky sex than in sporadic or exclusive relationships.

*Sex work is the problem* - Formal sex work is uncommon in these generalised epidemics. In Lesotho, fewer than 2% of men reported paying for sex in the previous year, although 29% reported multiple partners.<sup>7</sup> Nuanced economic support is an important enabler of regular concurrent partnerships and transactional sex, but the targeting of sex work in prevention campaigns has limited usefulness.

*Men are the problem* - The behaviour of men, including cross-generational and coercive sex, contributes substantially to the establishment of generalised epidemics. But a heterosexual epidemic requires some women to have multiple partners.<sup>3</sup> The importance of women in generalised epidemics is evidenced by the high proportion (sometimes the majority) of discordant couples in which the woman, not the man, is HIV positive (figure).<sup>5</sup>

*Adolescents are the problem* - Generalised epidemics span all reproductive ages. Although adolescent women are affected through sex with older men, HIV incidence increases in women in their 20s and later in life.<sup>8</sup> Men are infected at even older ages. Thus interventions in young people, including abstinence, although important, have limited usefulness.

*Poverty and discrimination are the problem* - These factors can surely engender risky sex. But HIV is paradoxically more common in wealthier people than in poorer people, perhaps because wealth and mobility support concurrent sexual partnerships.<sup>9</sup> Moreover, HIV has declined without major improvements in poverty and discrimination, notably in Zimbabwe (notwithstanding substantial economic and social distress).

*Condoms are the answer* - Condom use, especially by sex workers, is crucial to the containment of concentrated epidemics, and condoms help to protect some individuals. But condoms alone have limited impact in generalised epidemics. Many people dislike using them (especially in regular relationships), protection is imperfect, use is often irregular, and condoms seem to foster disinhibition, in which people engage in risky sex either with condoms or with the intention of using condoms.<sup>8</sup>

*HIV testing is the answer* - That learning one's HIV status (hopefully with counselling) should lead to behavioural change and reduced risk seems intuitive. However, real-world evidence of such change is discouraging, especially for the large majority who test negative.<sup>3</sup> Moreover any changes must be sustained for years. And very newly infected people, who are highly infectious, do not yet test HIV-positive.

*Treatment is the answer* - Theoretically, treatment and counselling might aid prevention by lowering viral levels (and infectiousness) in those treated, reducing denial about HIV, and promoting behavioural change. However, no clear effect has emerged. Indeed these salutary effects might be outweighed by negative effects, such as resumption of sexual activity once those on antiretrovirals feel well, and disinhibition when people realise that HIV might no longer be a death sentence.

*New technology is the answer* - Many resources are devoted to vaccines, **microbicides**, and prophylactic antiretrovirals. Unfortunately any success appears to be far off. Moreover, such innovations might be mainly targeted only at very high-risk populations, rely on behavioural compliance, and engender disinhibition.<sup>10</sup> Similarly, treatment of sexually transmitted infections to prevent HIV has been disappointing.<sup>11</sup> Even male circumcision, an already available, unmistakably effective, and compelling priority will take years to have additional substantial effect.

*Sexual behaviour will not change* - Actually, facing the prospect of deadly illness, many people will change. Homosexual men in the USA radically changed behaviour in the 1980s. And the reductions in HIV incidence in Kenya and eastern Zimbabwe were accompanied by large drops in multiple partners,<sup>8,12</sup> probably largely as a spontaneous reaction to fear.

Truthfully, our priority must be on the key driver of generalised epidemics - concurrent partnerships. Although many people sense that multiple partners are risky, they do not realise the particular risk of concurrent partnerships. Indeed, technical appreciation of their role is recent.<sup>6</sup> But partner limitation has also been neglected because of the culture wars between advocates of condoms and advocates of abstinence, because it smacks of moralising, because mass behavioural change is alien to most medical professionals, and because of the competing priorities of HIV programmes.

Fortunately we can enhance partner-limitation behaviour, akin to the behaviour change that many people have adopted spontaneously. State-of-the-art behaviour-change techniques, including explicit messages, that are sensitive to local cultures, can raise perception of personalised risk. Even modest reductions in concurrent partnerships could substantially dampen the epidemic dynamic. Other prevention approaches also have merit, but they can be much more effective in conjunction with partner-limitation. Now, more than 20 years into HIV prevention, we have to get it right.

**EDITOR'S NOTE: This article, including references, is available with a free subscription at the above website.**

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#### **4. PUBLISHED RESEARCH: MICROBICIDE-SPECIFIC**

**"HIV treatment proceeds as prevention research confounds"**

**Author(s):**

**Reference:** N/A 4(12):e347. Editorial.

**Published Abstract:** World AIDS Day, the annual December 1 commemoration, first took place in 1988 under the auspices of the Joint United Nations Programme on HIV/AIDS [1]. At that time few had recognized the epidemic's impending global scope or envisaged how to provide AIDS treatment in developing countries. During the previous year, the United States Food and Drug Administration (FDA) had licensed zidovudine (AZT), the first drug shown to be effective for treating HIV. AZT, which quickly became available in North America and Europe, provided modest hope for the first time since the initial reports of AIDS in 1981. Taken as a single drug every four hours round the clock, it could prolong life by half a year or more [2].

Twenty years later, HIV treatment has the potential to become one of medicine's success stories. Combination anti-HIV therapies, referred to generically as highly active antiretroviral therapy (HAART), began to appear around 1996. Although costly and not without adverse effects, these "cocktails" have proved so effective that many who narrowly escaped death from AIDS in the mid-1990s are now facing the usual health concerns of advancing age. Although emergence of drug-resistant virus creates ongoing challenges, HIV treatment has continued to advance, as evidenced by the development of more convenient treatment regimens, and by FDA approval in 2007 of drugs from two new mechanistic classes: the first integrase inhibitor and the first chemokine receptor blocker.

On the global scale, 2007 has seen further progress in the impressive effort to address financial and logistical barriers to providing HIV treatment in low-resource settings. Although some 5 million people remain in need of HAART, and a recent systematic review found that many who begin HAART in developing countries do not continue treatment [3], the fact that more than 2 million people in low- and middle-income countries are now receiving HAART marks significant progress.

In this context of global progress toward HIV treatment, the official theme of World AIDS Day 2007 appropriately calls on "Leadership" to "Keep the Promise" of universal access to HIV care and services.

Pounds of much-needed treatment, however, should not obscure the fact that precious ounces of prevention remain elusive: interrupting HIV transmission remains one of the world's greatest scientific challenges. Indeed, in contrast to the progress made in treatment, World AIDS Day 2007 marks the end of a particularly sobering year in HIV prevention science, particularly in the area of female-controlled methods, which have long been recognized as key to interrupting HIV transmission when social and economic disempowerment prevent women from insisting on condoms. January brought the announcement that two developing country trials of the vaginal **microbicide** cellulose sulfate had to be stopped because of an increased risk of HIV infection in women using the product [4,5]. The result was disappointingly reminiscent of the nonoxynol-9 vaginal **microbicide** trial that ended with a similar outcome in 2000 [6]. Another setback to female-controlled prevention came in July with the report that providing latex diaphragms and gel together with male condoms to women in southern Africa gave no additional protection against HIV compared with condoms alone [7]. September brought more bad news: the early cessation of a major international HIV vaccine trial when interim analysis found that the vaccine, Merck's trivalent adenovector product, appeared no better than placebo in preventing HIV infection [8]. Again the disappointment was familiar; in 2003 the first vaccine studies designed to assess protection against HIV in humans, using the VaxGen envelope products, were completed with no convincing

evidence of efficacy.

In the area of behavioral prevention, a 2007 systematic review of available reports [9] found that abstinence-only programs, incorporated into many US and developing country HIV programs as a condition of US government funding, have been ineffective in reducing HIV risk in high-income countries. However, a study of abstinence-plus programs (which promote condom use as an alternative when abstinence fails) found the latter programs to be more promising [10]. In 2007, US-supported treatment programs directly or indirectly provided HAART to more than a million people in developing countries, and provided more general HIV care and prevention services to millions more. To assure success in HIV prevention, it is time for leaders of the US effort to act on the scientific evidence and end political requirements for abstinence-only funding.

In perhaps the year's most convincing results regarding HIV prevention, clinical trials in Uganda and Kenya, confirming an earlier trial from South Africa [11], showed that circumcision of adult men reduced their risk of acquiring HIV by about half over the subsequent two years [12,13]. However, even if this level of protection can be realized in the face of uncertain acceptance rates for circumcision and despite increased risk taking that may result from expectations of protection following circumcision, the risk reduction for a given male would still be no better than that of condom use for those who will use them. In turn, the effectiveness of circumcision - hardly a recent surgical technique - invites comparison to state-of-the-art research in immunology and virology, which have yet to deliver anything close to a reliable 50% reduction in risk of acquiring HIV through sexual exposure. Despite efforts of thousands of volunteers and expenditures of many tens of millions of dollars on clinical prevention trials ending in 2007, protection against sexual acquisition of HIV remains decidedly low-tech and frustratingly fixated on the phallus.

In terms of short-term benefit, then, it could be argued that basic research funding should instead be redirected toward condom education programs. In the long term, however, more definitive prevention methods are desperately needed to bring the AIDS crisis to an end, and we must not give up working toward a breakthrough in prevention comparable to the treatment advances of the past decade. New **microbicides** and vaccines are being developed and tested, trials of pre-exposure prophylaxis are under way, and more basic research in HIV epidemiology and pathogenesis continues to advance.

The essential need for global dissemination and discussion of research reports is nowhere better illustrated than in the response to the vast complexity of the AIDS pandemic. PLoS Medicine has published many papers on HIV/AIDS, is featuring several new papers [14-20] in this World AIDS Day issue, and will publish several more over the coming weeks. For announcements and discussion of these upcoming articles in PLoS Medicine as well as papers on HIV/AIDS in PLoS ONE, we invite our readers to check, and comment via, the PLoS Medicine blog (<http://www.plos.org/cms/plosmedicine/>).

**"The microbicide tenofovir does not inhibit nucleic acid amplification tests for Chlamydia trachomatis and Neisseria gonorrhoeae in urine samples"**

**Author(s):** Wood BJ, Rizzo-Price P, Holden J, et al

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

<http://jcm.asm.org/cgi/content/abstract/JCM.01867-07v1?ct=ct>

**Published Abstract:** The potential inhibitory effect of Tenofovir and placebo were examined using: Becton Dickinson ProbeTec, Gen-Probe Aptima Combo2, and Roche Amplicor to detect *Chlamydia trachomatis* (CT) and *Neisseria gonorrhoeae* (NG). Concentrations, 5% to 0% of Tenofovir and placebo were added to dilutions of CT and NG. No appreciable inhibition was observed.

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

### "A systematic review of published evidence on intervention impact on condom use in sub-Saharan Africa and Asia"

**Author(s):** Foss AM, Hossain M, Vickerman PT, et al

**Reference:** N/A 83(7):510-16.

<http://sti.bmj.com/cgi/content/abstract/83/7/510?etoc>

**Published Abstract:** *Objective:* There has been much debate about the value of condoms in HIV/STI programming. This should be informed by evidence about intervention impact on condom use, but there is limited compiled literature. This review aims to quantify intervention impact on condom use in sub-Saharan Africa and Asia, in different types of partnership. *Methods:* A systematic review was conducted of papers published between 1998 and 2006 presenting evaluations of interventions involving condom promotion in sub-Saharan Africa and Asia. Data on reported postintervention levels of condom use, and various measures of changes in condom use, by partnership type, were compiled. *Results:* A total of 1374 abstracts were identified. Sixty-two met the inclusion criteria (42 reporting significant increases in condom use): 44 from sub-Saharan Africa and 18 from Asia. Many (19) reported on condom use in commercial sex (15 significant), six on use with casual partners (three significant), 11 on use in marital/steady partnerships (nine significant), 14 on use by youths (eight significant) and 20 combined partnership types (11 significant). There is substantial evidence of interventions targeted at sex workers and clients achieving large increases in condom use. Far less evidence exists of intervention impact on condom use in casual relationships. In primary partnerships, postintervention condom use was low unless one partner was knowingly HIV-infected or at high-risk, or avoiding pregnancy. Evaluations of interventions targeting youths recorded limited increases in condom use. *Conclusions:* The findings illustrate the range of evidence about postintervention condom use in different partnerships, and how patterns of use are influenced by partnership type and perceptions of risk. Where possible, intervention studies should also assess biological endpoints, since prevention of infection is the measure of most interest in the evaluation of condom promotion interventions.

## "Circumcision status and HIV infection among black and latino men who have sex with men in 3 US cities"

**Author(s):** Millett GA, Ding H, Lauby J, et al

**Reference:** N/A 46(5):643-50.

<http://www.jaids.org/pt/re/jaids/abstract.00126334-200712150-00017.htm;jsessionid=HNBc10nmvSQB7JpVJ1yYIkBfynVh9q2dfKV0kMQ1L1RwBpFQ3Swz!-1601909834!181195629!8091!-1>

**Published Abstract:** *Objective:* To examine characteristics of circumcised and uncircumcised Latino and black men who have sex with men (MSM) in the United States and assess the association between circumcision and HIV infection. *Methods:* Using respondent-driven sampling, 1154 black MSM and 1091 Latino MSM were recruited from New York City, Philadelphia, and Los Angeles. A 45-minute computer-assisted interview and a rapid oral fluid HIV antibody test (OraSure Technologies, Bethlehem, PA) were administered to participants. *Results:* Circumcision prevalence was higher among black MSM than among Latino MSM (74% vs. 33%; P (less than) 0.0001). Circumcised MSM in both racial/ethnic groups were more likely than uncircumcised MSM to be born in the United States or to have a US-born parent. Circumcision status was not associated with prevalent HIV infection among Latino MSM, black MSM, black bisexual men, or black or Latino men who reported being HIV-negative based on their last HIV test. Further, circumcision was not associated with a reduced likelihood of HIV infection among men who had engaged in unprotected insertive and not unprotected receptive anal sex. *Conclusions:* In these cross-sectional data, there was no evidence that being circumcised was protective against HIV infection among black MSM or Latino MSM.

## "Clinical trials and medical care: defining the therapeutic misconception"

**Author(s):** Henderson GE, Churchill LR, Davis AM, et al

**Reference:** N/A 4(11):e324.

<http://medicine.plosjournals.org/perlserv/?request=get-document&doi=10.1371%2Fjournal.pmed.0040324>

**Published Abstract:** *What Is Therapeutic Misconception?* For over three decades, bioethics scholarship and research ethics guidelines have identified concerns about the boundaries between research and standard clinical care [1,2]. Ethicists have argued that informed consent to participate in research should include clarification of the differences between these two activities [3-10]. In 1982, Appelbaum and colleagues reported on findings from interviews with patients with psychiatric disorders that documented failure to appreciate the difference between research and treatment, labeling the phenomenon "therapeutic misconception" (TM) [3]. Despite considerable empirical research on TM in the intervening years, a consistent definition has not emerged in the literature. Without such a definition, meaningful empirical work to measure and assess the prevalence of TM, or to test interventions to reduce it, is difficult to conduct. Progress is further impeded when studies use measures that reflect inconsistent definitions of research and clinical care, which are fundamental to the definition of TM. Scholars who have contributed to this literature, including this paper's authors, met at the University of North Carolina at Chapel Hill in September 2005 to address the debate on defining TM. The workshop included a University of North Carolina team funded to study TM in early-phase gene transfer research (R01 HG 02087) [11-17] and others from the fields of medicine,

oncology, public health, sociology, philosophy, anthropology, law, and bioethics. Following guidelines on scale development [18], we debated definitions based on the literature, evaluated questions that could be used in a TM scale, and participated in ongoing discussion during the following year. In this article, we summarize the controversies, propose a definition with specific dimensions, and describe how these dimensions can be operationalized to produce a valid measure of TM.

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

## **"Dendritic cells are less susceptible to human immunodeficiency virus type 2 (HIV-2) infection than to HIV-1 infection"**

**Author(s):** Duvall MG, Lore K, Blaak H, et al

**Reference:** N/A 81(24):13486-98. Melody G. Duvall,1,4 Karin LorÃ©,2,4 Hetty Blaak,

<http://jvi.asm.org/cgi/content/abstract/81/24/13486?etoc>

**Published Abstract:** Human immunodeficiency virus type 1 (HIV-1) infection of dendritic cells (DCs) has been documented in vivo and may be an important contributor to HIV-1 transmission and pathogenesis. HIV-1-specific CD4+ T cells respond to HIV antigens presented by HIV-1-infected DCs and in this process become infected, thereby providing a mechanism through which HIV-1-specific CD4+ T cells could become preferentially infected in vivo. HIV-2 disease is attenuated with respect to HIV-1 disease, and host immune responses are thought to be contributory. Here we investigated the susceptibility of primary myeloid DCs (mDCs) and plasmacytoid DCs (pDCs) to infection by HIV-2. We found that neither CCR5-tropic primary HIV-2 isolates nor a lab-adapted CXCR4-tropic HIV-2 strain could efficiently infect mDCs or pDCs, though these viruses could infect primary CD4+ T cells in vitro. HIV-2-exposed mDCs were also incapable of transferring virus to autologous CD4+ T cells. Despite this, we found that HIV-2-specific CD4+ T cells contained more viral DNA than memory CD4+ T cells of other specificities in vivo. These data suggest that either infection of DCs is not an important contributor to infection of HIV-2-specific CD4+ T cells in vivo or that infection of DCs by HIV-2 occurs at a level that is undetectable in vitro. The frequent carriage of HIV-2 DNA within HIV-2-specific CD4+ T cells, however, does not appear to be incompatible with preserved numbers and functionality of HIV-2-specific CD4+ T cells in vivo, suggesting that additional mechanisms contribute to maintenance of HIV-2-specific CD4+ T-cell help in vivo.

## **"Diaphragms and lubricant gel for prevention of HIV"**

**Author(s):**

**Reference:** N/A 370(9602):1823-24. Correspondence and Author reply.

**Published Abstract:**

**EDITOR'S NOTE: This weeks' Lancet featured correspondence and author's reply to the article "Diaphragm and lubricant gel for prevention of HIV in southern African women: a randomised controlled trial," which appeared in the 21 July 2007 issue of the Lancet. Below are links to both correspondence, the author's reply, and the original Lancet article to which all three refer.**

Author(s) Padian NS, van der Straten A, Ramjee G, the MIRA Team.

Reference: Diaphragm and lubricant gel for prevention of HIV acquisition in southern African women: a randomised controlled trial. Lancet 2007; published online July 13.

<http://www.ncbi.nlm.nih.gov/sites/entrez?db=pubmed&uid=17631387&cmd=showdetailview&indexed=google>

Author(s): Stein Z, Glymour MM

Reference: Lancet. 2007 Dec 01;370(9602):1823. Correspondence.

<http://www.thelancet.com/journals/lancet/article/PIIS0140673607617656/fulltext>

Author(s): Shelton JD

Reference: Lancet. 2007 Dec 01;370(9602):1823. Correspondence.

<http://www.thelancet.com/journals/lancet/article/PIIS0140673607617644/fulltext>

Authors' reply

Author(s): Jewell N, van der Straten A, Montgomery ET, et al.

Reference: Lancet. 2007 Dec 01;370(9602):1823-24.

<http://www.thelancet.com/journals/lancet/article/PIIS0140673607617668/fulltext>

### **"Frequent douching and clinical outcomes among HIV-infected women"**

**Author(s):** Clark RA, Theall KP, Amedee AM, et al

**Reference:** N/A 34(12):985-90.

<http://www.stdjournal.com/pt/re/std/abstract.00007435-200712000-00009.htm;jsessionid=HTmTHBTFIT7JYGMQXHSzSSGrRQcvb366s85cy5P2qlGJb6QGmQlbI65375592!181195628!8091!-1>

**Published Abstract:** *Objective:* To determine the prevalence of douching among a cohort of HIV-infected women and to examine clinical outcomes associated with frequent douching—namely bacterial vaginosis, presence of a sexually-transmitted infections, and genital tract HIV-1 RNA shedding. *Study Design:* Participants included a concurrent cohort of 187 women attending an HIV outpatient clinic in New Orleans, LA. Subjects underwent clinical examinations and answered questions in a computer-assisted survey at each visit. *Results:* At baseline, 1-, and 3-month follow-ups, 64.2%, 56.5%, and 54.7% of women, respectively, indicated that they douched. In multivariable analyses, douching less than 1 time a month was independently associated with the outcomes of bacterial vaginosis and presence of a selected sexually transmitted infection (*Trichomonas vaginalis*, *Neisseria gonorrhoea*, or *Chlamydia trachomatis*). Although not significant, women who douched less than 1 time a month were also twice as likely to have genital tract HIV-1 RNA shedding as nondouchers. *Conclusions:* This is the first study performed in women infected with HIV to link a significant dose-response relationship between douching and the clinical outcomes of bacterial vaginosis and presence of a sexually transmitted infection, and to examine the association between

douching and genital tract HIV-1 RNA shedding.

**"Interventions among male clients of female sex workers in Benin, West Africa: an essential component of targeted HIV preventive interventions"**

**Author(s):** Lowndes CM, Alary M, Labbe AC, et al

**Reference:** N/A 83(7):577-81.

<http://sti.bmj.com/cgi/content/abstract/83/7/577?etoc>

**Published Abstract:** *Objectives:* To assess the impact of interventions targeted towards female sex workers (FSWs) and their male clients on client HIV/STI prevalence and sexual behaviour. *Methods:* From 1993 to 2006, an HIV/STI preventive intervention focusing on condom promotion and STI care was implemented among FSWs in Cotonou, Benin, and then expanded to cover their male sexual partners in 2000. The interventions were scaled up to five other cities of Benin in 2001-2002. Serial cross-sectional surveys of HIV/STI prevalence and sexual behaviour were carried out among clients in Cotonou in 1998, 2002 and 2005; and in the five other cities (O/Cotonou) in 2002 and 2005. *Results:* Significant declines in gonorrhoea prevalence among clients of FSWs: Cotonou, from 5.4% in 1998 to 1.6% in 2005; O/Cotonou: from 3.5% in 2002 to 0.59% in 2005. Chlamydia prevalence also declined O/Cotonou, from 4.8% to 1.8%, while HIV prevalence remained stable. Reported condom use by clients with both FSWs and casual non-FSW partners, but not regular partners, increased significantly. While condom use at last sex with an FSW was similar in Cotonou to O/Cotonou around the time of implementation of the interventions (56% in 1998 vs 49% in 2002, respectively), it had risen to similar levels by 2005 (95% and 96%, respectively). *Conclusions:* These results demonstrate that it is possible to implement preventive and clinical services for clients of FSWs, and suggest that such interventions, integrated with those targeted towards FSWs, can have a significant effect on sexual behaviour and STI prevalence (particularly gonorrhoea) among this population.

**"Longitudinal association between hormonal contraceptives and bacterial vaginosis in women of reproductive age"**

**Author(s):** Riggs M, Klebanoff M, Nansel T, et al

**Reference:** N/A 34(12):954-59.

<http://www.stdjournal.com/pt/re/std/abstract.00007435-200712000-00004.htm;jsessionid=HTmFfc0Kyhy3qbNmcMkBfxVPmppcLKKTbt02yxnvVzrPxzqyn4hQ!65375592!181195628!8091!-1>

**Published Abstract:** *Objectives:* This study examined whether hormonal contraceptive use is associated with diagnosis of bacterial vaginosis (BV) over 1 year. *Study Design:* A total of 3077 women of reproductive age were recruited from gynecologic and family planning clinics for a 1-year prospective longitudinal study. Data collected over 5 visits included demographics, health and hygiene behaviors, and gynecological exams. Gram stains were used to

quantify vaginal flora. *Results:* There was a decreased risk of overall BV prevalence among oral contraceptive users (odds ratio, OR 0.76; confidence interval, CI 0.63-0.90) and among those using hormonal injection/implant (OR 0.64; CI 0.53-0.76). An increased risk for BV prevalence (OR 1.38; CI 1.11-1.71) and incidence (OR 1.43; 1.02-2.07) was observed among those subjects who had tubal ligation. Greater remission of BV was found among those using hormonal injection or implant (OR 1.67; CI 1.23-2.27) whereas less remission occurred among those subjects who had tubal ligation (OR 0.56; CI 0.39-0.80). *Conclusions:* Hormonal contraceptive use is associated with a decreased risk of BV.

### **"Risk factors for herpes simplex virus type 2 and HIV among women at high risk in northwestern Tanzania: preparing for an HSV-2 intervention trial"**

**Author(s):** Watson-Jones D, Weiss HA, Rusizoka M, et al

**Reference:** N/A 46(5):631-42.

<http://www.jaids.org/pt/re/jaids/abstract.00126334-200712150-00016.htm;jsessionid=HNQXrG9whHf5dvBJS2N6cKvGRjrKBSC9jBLZ2xx8S6nQn3YChY8!65375592!181195628!8091!-1>

**Published Abstract:** *Objectives:* To determine prevalence of and risk factors for herpes simplex virus type 2 (HSV-2) and HIV among women being screened for a randomized, controlled trial of HSV suppressive therapy in northwestern Tanzania. *Methods:* Two thousand seven hundred nineteen female facility workers aged 16 to 35 were interviewed and underwent serological testing for HIV and HSV-2. Factors associated with HSV-2 and HIV in women aged 16 to 24 were examined using logistic regression to estimate odds ratios (OR) and 95% confidence intervals (CI). *Results:* HSV-2 seroprevalence was 80%, and HIV seroprevalence was 30%. Among women aged 16 to 24, both infections were significantly and independently associated with older age, being a bar worker, working at a truck stop, and having more lifetime sexual partners. HSV-2 infection was also associated with lower socioeconomic status, increased alcohol intake, younger age at first sex, inconsistent condom use, and vaginal douching. There was a strong association between the 2 infections after adjustment for other factors (OR = 4.22, 95% CI: 2.6 to 6.9). *Conclusions:* Female facility workers in northwestern Tanzania are vulnerable to HSV-2 and HIV infections. Programs designed to increase safer sexual behavior and reduce alcohol use could be effective in reducing HSV-2 incidence and, in turn, HIV infection. This is a suitable population for an HSV suppressive therapy trial.

### **"Systemic and mucosal infection program protective memory CD8 T cells in the vaginal mucosa"**

**Author(s):** Suvas PK, Dech HM, Sambira F, et al

**Reference:** N/A 179(12):8122-27.

<http://www.jimmunol.org/cgi/content/abstract/179/12/8122?etoc>

## Published Abstract:

Whether mucosal immunization is required for optimal protective CD8 T cell memory at mucosal surfaces is controversial. In this study, using an adoptive transfer system, we compare the efficacy of two routes of acute lymphocytic choriomeningitis viral infection on the generation, maintenance, and localization of Ag-specific CD8 T cells in tissues, including the vaginal mucosa. Surprisingly, at day 8, i.p. infection results in higher numbers of Ag-specific CD8 T cells in the vaginal mucosa and iliac lymph node, as well as 2-3x more Ag-specific CD8 T cells that coexpress both IFN- and TNF- in comparison to the intranasal route of infection. Expression of the integrin/activation marker CD103 (E $\alpha$ Z $\beta$ 7) is low on vaginal mucosal Ag-specific CD8 T cells in comparison to gut mucosal intraepithelial lymphocytes. At memory, no differences are evident in the number, cytokine production, or protective function of Ag-specific CD8 T cells in the vaginal mucosa comparing the two routes of infection. However, differences persist in the cytokine profile of genital tract vs peripheral Ag-specific CD8 T cells. So although the initial route of infection, as well as tissue microenvironment, appear to influence both the magnitude and quality of the effector CD8 T cell response, both systemic and mucosal infection are equally effective in the differentiation of protective memory CD8 T cell responses against vaginal pathogenic challenge.

## "When do HIV-infected women disclose their HIV status to their male partner and why? A study in a PMTCT programme, Abidjan"

**Author(s):** Brou H, Djohan G, Becquet R, et al

**Reference:** N/A 4(12):e342.

<http://medicine.plosjournals.org/perlserv/?request=get-document&doi=10.1371/journal.pmed.0040342>

**Published Abstract:** *Background* In Africa, women tested for HIV during antenatal care are counselled to share with their partner their HIV test result and to encourage partners to undertake HIV testing. We investigate, among women tested for HIV within a prevention of mother-to-child transmission of HIV (PMTCT) programme, the key moments for disclosure of their own HIV status to their partner and the impact on partner HIV testing. *Methods and Findings* Within the Ditrane Plus PMTCT project in Abidjan, 546 HIV-positive and 393 HIV-negative women were tested during pregnancy and followed-up for two years after delivery. Circumstances, frequency, and determinants of disclosure to the male partner were estimated according to HIV status. The determinants of partner HIV testing were identified according to women's HIV status. During the two-year follow-up, disclosure to the partner was reported by 96.7% of the HIV-negative women, compared to 46.2% of HIV-positive women ( $X^2 = 265.2$ , degrees of freedom [df] = 1,  $p$  (less than) 0.001). Among HIV-infected women, privileged circumstances for disclosure were just before delivery, during early weaning (at 4 mo to prevent HIV postnatal transmission), or upon resumption of sexual activity. Formula feeding by HIV-infected women increased the probability of disclosure (adjusted odds ratio 1.54, 95% confidence interval 1.04-2.27, Wald test = 4.649, df = 1,  $p = 0.031$ ), whereas household factors such as having a co-spouse or living with family reduced the probability of disclosure. The proportion of male partners tested for HIV was 23.1% among HIV-positive women and 14.8% among HIV-negative women ( $X^2 = 10.04$ , df = 1,  $p = 0.002$ ). Partners of HIV-positive women who were informed of their wife's HIV status were more likely to undertake HIV testing than those not informed (37.7% versus 10.5%,  $X^2 = 56.36$ , df = 1,  $p$  (less than) 0.001). *Conclusions* In PMTCT programmes, specific psychosocial counselling and support should be provided to women during the key moments of disclosure of HIV status to their partners (end of pregnancy, weaning, and resumption of sexual activity). This support could contribute

to improving women's adherence to the advice given to prevent postnatal and sexual HIV transmission.

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

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## 6. HIV/AIDS VACCINES

### "Antibody-based HIV-1 vaccines: recent developments and future directions"

**Author(s):** Montefiori D, Sattentau Q, Flores J, et al

**Reference:** N/A 4(12):e348. A summary report from a Global HIV Vaccine Enterprise Working Group.

<http://medicine.plosjournals.org/perlserv/?request=get-document&doi=10.1371/journal.pmed.0040348>

**Published Abstract:** The Global HIV Vaccine Enterprise convened a two-day workshop in May of 2007 to discuss humoral immune responses to HIV and approaches to design vaccines that induce viral neutralizing and other potentially protective antibody responses. The goals of this workshop were to identify key scientific issues, gaps, and opportunities that have emerged since the Enterprise Strategic Plan was first published in 2005 [1], and to make recommendations that Enterprise stakeholders can use to plan new activities.

Most effective viral vaccines work, at least in part, by generating antibodies that inactivate or neutralize the invading virus, and the existing data strongly suggest that an optimally effective HIV-1 vaccine should elicit potent antiviral neutralizing antibodies. However, unlike acute viral pathogens, HIV-1 chronically replicates in the host and evades the antibody response. This immune evasion, along with the large genetic variation among HIV-1 strains worldwide, has posed major obstacles to vaccine development. Current HIV vaccine candidates do not elicit neutralizing antibodies against most circulating virus strains, and thus the induction of a protective antibody response remains a major priority for HIV-1 vaccine development. For an antibody-based HIV-1 vaccine, progress in vaccine design is generally gauged by *in vitro* assays that measure the ability of vaccine-induced antibodies to neutralize a broad spectrum of viral isolates representing the major genetic subtypes (clades) of HIV-1 [2]. Although it is not known what magnitude and breadth of neutralization will predict protection in vaccine recipients, it is clear that current vaccine immunogens elicit antibodies that neutralize only a minority of circulating isolates. Thus, much progress needs to be made in this area. Also, though virus neutralization is considered a critical benchmark for a vaccine, this may not be the only benchmark for predicting success with antibody-based HIV-1 vaccine immunogens.

The main targets for neutralizing antibodies to HIV-1 are the surface gp120 and trans-membrane gp41 envelope glycoproteins (Env) that mediate receptor and coreceptor binding and the subsequent membrane fusion events that allow the virus to gain entry into cells [3]. Antibodies neutralize the virus by binding these viral spikes and blocking virus entry into susceptible cells, such as CD4+ T cells [4,5]. In order to chronically replicate in the host, the virus exploits several mechanisms to shield itself against antibody recognition, including a dense outer coating of sugar molecules (N-linked glycans) and the strategic positioning of cysteine-cysteine loop structures on the gp120 molecule [6-8]. These shielding mechanisms, although highly effective, have vulnerabilities imposed by fitness constraints.

Information on the precise location and molecular structure of these vulnerable regions could be valuable for the rational design of improved vaccine immunogens.

Participants in the workshop identified four areas that, if given proper attention, could provide key information that would bring the field closer to an effective antibody-based HIV-1 vaccine: (1) structure-assisted immunogen design, (2) role of Fc receptors and complement, (3) assay standardization and validation, and (4) immunoregulation of B cell responses.

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

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## 7. OTHER PREVENTION APPROACHES

### "China launches first major safe sex TV campaign"

**Date:** 06 December 2007

**Source:** Reuters

**Author(s):** Ben Blanchard

<http://www.alertnet.org/thenews/newsdesk/PEK36497.htm>

China rolled out its first major television campaign on Thursday to promote condom use to fight the spread of HIV/AIDS, now mostly being transmitted by sex in the world's most populous country. The short public service announcements will mainly be shown on screens in buses, trains and planes, on the Internet, in entertainment venues, and on some state television channels.

They will target the young and China's huge floating population of migrant workers, using celebrities including Hong Kong action film star Jackie Chan and Chinese folk singer Peng Liyuan, wife of rising political star Xi Jinping.

"It marks a new era in talking frankly and candidly about these issues, which used to be avoided," said UNDP country director Subinay Nandy. "This initiative is very timely and is very valid for the epidemic situation in China today," he told a news conference.

China will have an estimated 50,000 new HIV infections in 2007, compared with 70,000 in 2005, according to a report by the State Council (Cabinet) and the United Nations last week. That means the country will have about 700,000 people living with HIV/AIDS this year, up from an earlier estimate of 650,000. The new education push is designed to slow that growth further.

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

## **"Condom maker CEO voices 'safe sex'"**

**Date:** 06 December 2007

**Source:** *The Korea Times*

**Author(s):** Ryu Jin

[http://www.koreatimes.co.kr/www/news/special/2007/12/178\\_15059.html](http://www.koreatimes.co.kr/www/news/special/2007/12/178_15059.html)

In a country where sex is still a taboo word, it would not be easy to sell condoms. But, here is a CEO who struggles not only to promote his company's sales but also raise public awareness of so-called safe sex.

UNIDUS President Kim Sung-hoon, who took office as the chief of his company in June last year at the age of 39, stressed in an interview with *The Korea Times* that condoms are the best way to protect oneself from disease as well as unwanted pregnancy.

Listed on the tech-heavy KOSDAQ, UNIDUS has recently emerged as the world's No. 1 condom maker in terms of sales and production, accounting for more than 65 percent of the domestic market and over 30 percent of the global market.

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

## **"HIV-positive women carry extra burden: Activists"**

**Date:** 06 December 2007

**Source:** *The Jakarta Post*

<http://www.thejakartapost.com/yesterdaydetail.asp?fileid=20071206.D06>

HIV-positive women struggle more than their male counterparts as they experience more discrimination and have to take care of their families, an NGO says.

"An HIV-positive mother must provide medicine and powdered milk to prevent her child from being exposed to HIV," Husein Habsyi, deputy head of Pelita Ilmu Foundation (YPI), said during a charity event for HIV-positive women and children to commemorate World AIDS Day on Dec. 1.

The event, which attracted more than 200 guests, was the first of its kind to be held by YPI and the Indonesian Positive Women's Association (IPPI). It was held to encourage people to support women and children with HIV and provide a chance for HIV-positive women to show their skills.

"We want to initiate change through a fund-raising activity like this, which provides opportunities for HIV-positive women to be more independent."

Shania, not her real name, an HIV-positive woman who joined YPI in 2005, said she was pleased to see so many people care about HIV women.

"It's a chance for me to express myself and send the message to every woman out there that HIV targets everyone, no matter who you are. You can be infected by your own husband," she said.

Data from the Ministry of Health in June indicates there are more than 1,900 HIV-positive women in the country. According to Prof. DR. Samsuridjal Djauzi, the founder of YPI, 80 percent of these women are housewives who were infected by their husbands.

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

### **"Traditional marriages ignore HIV/AIDS threat"**

**Date:** 06 December 2007

**Source:** *IRINNews.org*

<http://www.alertnet.org/thenews/newsdesk/IRIN/75e805ebba91eef87bea083dca6abc02.htm>

Bound by 'watta satta', a cultural tradition of exchanged marriage between two families, Nuzhat (not her real name), 22, cannot disclose her HIV status.

"I know well what will happen - I'll be thrown out of my husband's home and my own family will never accept me either. It will also mean my brother's home will be ruined. His wife is my husband's sister and she, too, will be sent packing. In any case, where will I go?" she asked in Karachi, provincial capital of Sindh Province in southeastern Pakistan.

The tradition of watta satta, which literally means 'give and take', or 'throwing a stone and receiving something back', describes the exchange of brides between families, in which a brother and sister from one family are married to a pair from another family, often close relatives.

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

### **"One in three in G7 ignorant about AIDS: survey"**

**Date:** 29 November 2007

**Source:** *Reuters*

**Author(s):** Patrick Worsnip

<http://www.reuters.com/article/healthNews/idUSN2920731020071129?feedType=RSS&feedName=healthNews>

One in three adults in the world's top industrial democracies say they know little or nothing about AIDS, a disease thought to have killed more than 28 million people in the past 26 years, a poll showed on Thursday.

But the survey, carried out by Ipsos for the World Vision charity, found that in the seven countries studied, 44 percent of respondents would be willing to pay more taxes to combat AIDS, including 50 percent in the United States.

More than 3,500 people in the United States, Canada, Britain, France, Germany, Italy and Japan -- the Group of Eight countries minus Russia -- were interviewed for the survey, released ahead of U.N. World AIDS Day on Saturday.

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

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## 8. POLITICS AND POLICY

### FDA Media Coverage

**EDITOR'S NOTE: Multiple articles appeared in the news recently regarding FDA and its current activities, mostly surrounding the release of the FDA Science and Mission at Risk report, which can be found at [http://www.fda.gov/ohrms/dockets/ac/07/briefing/2007-4329b\\_02\\_00\\_index.html](http://www.fda.gov/ohrms/dockets/ac/07/briefing/2007-4329b_02_00_index.html). Links to the articles are outlined below.**

FDA Needs More Money and Staff, Report Finds

Justin Blum

30 November 2007

*The Washington Post*

<http://www.washingtonpost.com/wp-dyn/content/article/2007/11/29/AR2007112902202.html?referrer=emailarticle>

Report: FDA so underfunded, consumers are put at risk

Julie Schmit

02 December 2007

*USA Today*

[http://www.usatoday.com/news/washington/2007-12-02-fda\\_N.htm?POE=click-refer](http://www.usatoday.com/news/washington/2007-12-02-fda_N.htm?POE=click-refer)

FDA science dearth puts public health at risk

Kim Dixon

03 December 2007

Reuters

[http://today.reuters.com/news/ArticleNews.aspx?type=scienceNews&storyID=2007-12-03T233820Z\\_01\\_N03444004\\_RTRUKOC\\_0\\_US-FDA-FLAWS.xml](http://today.reuters.com/news/ArticleNews.aspx?type=scienceNews&storyID=2007-12-03T233820Z_01_N03444004_RTRUKOC_0_US-FDA-FLAWS.xml)

Think tank asks FDA to purge conflicts

4 December 2007

FiercePharma

<http://www.fiercepharma.com/story/think-tank-asks-fda-purge-conflicts/2007-12-04>

## "Haitian-Americans fault report on spreading of AIDS"

**Date:** 01 December 2007

**Source:** *South Florida Sun-Sentinel*

**Author(s):** Ruth Morris

<http://www.sun-sentinel.com/features/health/sfl-flrnhiv1201pndec01,0,2808001.story>

Haitian-Americans are calling for an independent review of an AIDS study they say again stigmatizes them in the spread of HIV.

Activists, lawyers and health workers say the new research, based on genetic analysis of blood samples from three early Haitian patients in South Florida, could bring back discrimination they endured in the early 1980s. At that time, health officials singled out Haitians as being at increased risk for the virus that causes AIDS and banned them from donating blood.

The controversy around the new study "HIV-1 subtype CRF01\_AG" by evolutionary biologist Michael Worobey of the University of Arizona "overlaps with the good news last week that HIV is actually less prevalent globally than originally thought, and with World AIDS Day, which is observed around the world today.

But Haitian-Americans in South Florida say the Worobey report reopens an old wound.

"My initial reaction: This is just more of the same," said Jeff Cazeau, president of the Haitian Lawyers Association, of the Worobey study.

By comparing analysis of the three 25-year-old blood samples to others from around the world, the report asserts today's most widespread subtype of HIV emerged in Haiti in the 1960s, then spread to the United States a few years later. The timeline suggests to many that Haiti was a stepping-stone for the infection on its journey from Africa to the United States, but it does not conclude a Haitian immigrant brought the disease to the United States.

Cazeau said his group is seeking records from the Centers for Disease Control and Prevention to determine whether Worobey's team were authorized to use the blood samples at the root of the research.

Haitian physicians, meanwhile, have been encouraging scientists to take a second look at the data.

"Haitians historically have been used as scapegoats," said Marleine Bastien, a Haitian-American activist who cared for Haitian immigrant patients in South Florida in the 1980s as a clinical social worker.

The current sharp response to the study derives from abuses from that time, she said, when Haitians were tested for HIV at higher rates than other people, and then blamed for bringing the disease to South Florida shores.

"This had a devastating impact. Haitians were fired from employment. They were denied access to housing," she said.

"Calling someone Haitian became the worst curse."

Creole radio host Ancy Louis, of Greenacres, said he doubted the findings would bring a new stigma on his community, however, since people are better educated on AIDS today.

"We're becoming more mature. Everything is about education," he said.

The study, published a month ago in the Proceedings of the National Academy of Sciences, also notes a "high prevalence" of AIDS in Haitian immigrants in the United States soon after the infection was identified.

Eventually health officials came up with the "four H club" to denote risk factors: hemophilia, homosexuality, heroin use and being Haitian.

Dr. Art Fournier, associate dean of community health at the University of Miami, noted many Americans traveled to Haiti as sex tourists in the 1960s and '70s, and could easily have brought HIV back with them.

"We have to move beyond medical 'detectivism,'" said Fournier, author of *The Zombie Curse on HIV in Haiti*. "It's not about nationality. It's that the people who were infected were poor, therefore exploited, therefore infected."

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## 9. PHARMACEUTICAL INDUSTRY

### "92 medicines and vaccines now in development for HIV/AIDS"

**Date:** 20 November 2007

**Source:** *PhRMA*

[http://www.phrma.org/news\\_room/press\\_releases/92\\_medicines\\_and\\_vaccines\\_now\\_in\\_development\\_for\\_hiv%10aids/](http://www.phrma.org/news_room/press_releases/92_medicines_and_vaccines_now_in_development_for_hiv%10aids/)

Pharmaceutical researchers are testing 92 medicines and vaccines to treat or prevent HIV/AIDS and related conditions, according to a report released today by the Pharmaceutical Research and Manufacturers of America

(PhRMA). December 1 marks the 20th anniversary of "World AIDS Day" - a global awareness campaign that originated at the 1988 World Summit of Ministers of Health on Programmes for AIDS Prevention.

"We are greatly encouraged by the new, critically-important medicines and vaccines in development to treat and prevent HIV infection," says PhRMA President and CEO Billy Tauzin. "Pharmaceutical researchers are continuing their efforts to develop new therapies and vaccines to improve and lengthen the lives of HIV-infected patients."

The report found that of the 92 products in development, researchers are studying 20 vaccines and 46 antivirals. These drugs are either in human clinical trials or await approval by the U.S. Food and Drug Administration.

The report also lists 30 medicines to treat HIV/AIDS that have been approved since the virus that causes AIDS was first identified more than 20 years ago. The first such medicine was developed in 1987, just four years after the HIV virus was identified. The increased availability and utilization of newer prescription medicines has helped to reduce the U.S. death rate from AIDS substantially in recent years, according to government statistics.

Despite that progress, AIDS remains a devastating and growing worldwide health problem in developing countries, particularly in sub-Saharan Africa, China, India and the Russian Federation. According to the Joint United Nations Programme on HIV/AIDS, an estimated 32.7 million people worldwide lived with HIV at the end of 2006.

This year, that figure grew to an estimated 33.2 million people living with HIV, with an estimated 2.1 million people newly infected in 2007.

From 2000 to 2006, America's pharmaceutical research companies contributed more than \$6.7 billion to improve health care in the developing world, according to the International Federation of Pharmaceutical Manufacturers and Associations. The projects they underwrote included building clinics to treat patients with HIV/AIDS, education and prevention programs, initiatives to prevent mother-to-child transmission of HIV, and donations of medicines for AIDS and related diseases. Companies also provide AIDS drugs at significantly reduced prices in many countries.

"With HIV/AIDS medicines, a disease that was once a virtual death sentence can now be controlled and treated as if it were a chronic disease," adds Tauzin. "And the new medicines our scientists are working on right now bring hope for even more promising results in the future."

**EDITOR'S NOTE: The report mentioned in the above article is available at**  
**<http://www.phrma.org/files/Meds%20in%20Development%20for%20HIV%20AIDS.pdf>**

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## **10. ANNOUNCEMENTS**

**BIO, BVGH and Gates Foundation to Sponsor Partnering for Global Health Forum 2008**

[www.pghforum.org](http://www.pghforum.org)

The Biotechnology Industry Organization (BIO), BIO Ventures for Global Health (BVGH) and the Bill & Melinda Gates Foundation will co-sponsor the Partnering for Global Health Forum 2008, to be held March 10-12 in Washington, DC. The international partnering meeting will focus on opportunities for the biotechnology industry to help accelerate the development of medicines for neglected diseases of the developing world.

"Biotechnology holds the key to drug development for neglected diseases. Through this meeting we are opening up a dialogue to fully realize the enormous potential for biotech to help to save and transform lives in developing countries," said Jim Greenwood, president and CEO of BIO.

Attendees will address the pressing needs for innovation and explore new avenues for progress through lessons learned, market incentives, innovative business models and potential partnership meetings.

"The Partnering for Global Health Forum will bring together leaders in industry and global health to discuss how biotech's assets can best be leveraged to address the global health innovation gap and create the next generation of medicines for developing world diseases," said BVGH President and CEO Dr. Christopher D. Earl.

The Forum will feature:

- \* An open exchange with world-renowned leaders in global health, industry, government and the donor community
- \* Opportunities to meet one-on-one with leading companies, researchers, donors and investors
- \* Presentations from innovators pursuing technologies and products applicable to diseases of the developing world
- \* Perspectives from public and private funders supporting global health R&D

"Biotechnology companies have an essential role to play in global health," said Dr. Tachi Yamada, president of the Gates Foundation's Global Health Program. "We hope this partnering meeting will help more companies get involved in research to fight the world's most serious and neglected diseases."

For more information go to [www.pghforum.org](http://www.pghforum.org)

## **FDA Launches a Search for Director, Center for Drug Evaluation and Research (CDER)**

[www.usajobs.gov/](http://www.usajobs.gov/)

FDA has launched a nationwide search for Director, Center for Drug Evaluation and Research (CDER). The open period for applications is Tuesday, November 27, 2007, to Friday, February 1, 2008. The detailed job announcement and instructions for applying are available on the USAJOBS site (<http://www.usajobs.gov/>). See Job Announcement Number FDA-AD-2008-01.

## IRMA Announces John Shaw Memorial Scholarship Recipients

[www.irmwg.com](http://www.irmwg.com)

The International Rectal **Microbicide** Advocates is pleased to announce the recipients of John Shaw Memorial Scholarships, designed to assist advocates in attending the **Microbicide** 2008 conference in New Delhi, February 24 - 27, 2008.

Congratulations to:

Kadiri Etsegbe Audu - Lagos, Nigeria

Leonardo Coleman - Los Angeles, USA

Nesha Haniff - Ypsilanti, USA

Marc-Andre LeBlanc - Ottawa, Canada

Frank Gisha Mugisha - Kigali, Rwanda

William O'Brien - Boston, USA

Olanrewaju Olusola Onigbogi - Ibadan, Nigeria

Roy Wadia - Vancouver, Canada

John Shaw was a valued, enthusiastic and delightful member of the IRMA Steering Committee for over a year. He passed away Thursday, September 27, 2007. An LGBTQ/human rights advocate for over 20 years, John was also a Person With AIDS since at least 1990. IRMA created the John Shaw Memorial Scholarship Fund in his honor.

***EDITOR'S NOTE: Please visit the above website for more information about John Shaw and the Memorial Scholarship.***

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- In Vitro Drug Penetration Studies - At Dow we conduct unique in vitro studies to screen multiple prototype formulations. With topical dermatological products, it is imperative that the formulation used in early non-clinical and clinical studies be very close to the final commercial formulation.
- Clinical Manufacturing - Topical products are our focus. We have broad experience taking semisolid and liquid topical dosage forms through process development, scale-up and technology transfer - so we are very good at solving the problems that can occur. In the past 3 years alone, we have manufactured clinical supplies for ~ 75 clients..
- Clinical Labeling - Accurate labeling of your clinical supplies is of critical importance to your Program. Our clients rely on the experienced labeling and distribution team at Dow to label their supplies accurately every time and to deliver those supplies to the clinical sites on time.

## **Second Annual Clinical Trials Asia: 26-28 March 2008**

[http://www.tri-conference.com/08\\_clo.asp](http://www.tri-conference.com/08_clo.asp)

The Second Annual Clinical Trials Asia Conference: Strategies for Planning, Placing and Implementing Clinical Trials in India, China and Southeast Asia will take place 26-28 March 2008 in San Francisco, CA.

### *SESSIONS:*

- Designing and Planning Trials in India, China and Southeast Asia
- Managing the Ethical Review Committee Process
- Safety Reporting and Implementation of Pharmacovigilance Practices at Indian Sites
- Effectively Identifying, Selecting and Engaging Clinical Sites
- Navigating the Regulatory Landscape throughout Asia
- Strategic and Tactical Considerations when Designing and Conducting Trials in Asia: Learning from Others
- Overcoming Logistics, Managing Partners and Ensuring Compliance

### *INTERACTIVE PANELS:*

- Utilizing and Integrating Local Clinical Data from Asia to Mutually Support Global and Regional Applications
- Effectively Identifying, Selecting and Engaging Clinical Sites
- Navigating the Regulatory Landscape throughout Asia
- Realistic Opportunities and Main Challenges to Conducting Trials in India, China and Southeast Asia

## **WHO Global Strategy for the Prevention and Control of Sexually Transmitted Infections: 2006-2015**

<http://www.who.int/reproductive-health/stis/docs/stiskeymsgs.pdf>

Nearly a million people acquire a sexually transmitted infection (STI), including the human immunodeficiency virus (HIV), every day. The Global strategy has two components: technical and advocacy. The technical content of the strategy deals with methods to promote healthy sexual behaviour, protective barrier methods, effective and accessible care for STIs, and the upgrading of monitoring and evaluation of STI control programmes. The steps needed to develop health systems capacity to deliver the programme are explained. Emphasis is placed on a public health approach based on sound scientific evidence and cost-effectiveness. A section on advocacy offers advice to programme managers on approaches to mobilizing the high-level political commitment that forms the essential foundation for an accelerated response.

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