



ALLIANCE FOR MICROBICIDE DEVELOPMENT

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

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

Its purpose is to:

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

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

The Digest is produced in a web-based format. Readers can view complete issues of the Digest or search by keyword for individual articles at http://www.microbicide.org/cs/weekly_news_digest. If you would like to be removed from the Digest distribution list, please send an email to digest@microbicide.org. We welcome comments, questions, and ideas about other microbicide-relevant topics we might cover, services we might provide, and better ways of providing them!

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1. MEDIA COVERAGE OF MICROBICIDES

"Treatment and prevention exchange vows at international conference"

Date: 15 August 2008

Source: *Science*. 15 August 2008;321(5891):902-903. *News of the Week*.

Author(s): Joh Cohen

<http://www.sciencemag.org/cgi/content/full/321/5891/902>

AIDS researchers have long argued that HIV prevention and treatment efforts should go hand in hand, but they rarely do. Their fickle relationship received intense scrutiny at the XVII International AIDS Conference held here last week. "They keep going to the altar," said Myron "Mike" Cohen of the University of North Carolina (UNC), Chapel Hill, in a plenary presentation. "They never get married. They have to get married today."

More than 20,000 researchers, health care workers, representatives from hard-hit communities, and activists attended the conference, which had never been held in Latin America before. The meeting ran 3 to 8 August, and about one-fourth of the participants came from the region.

As usual at these gatherings, science shared the limelight with diverse issues such as scaling up access to anti-HIV drugs, the increasing criminal prosecution of people who infect others, and the need for countries to address their epidemics in ostracized groups. Protests were more muted than in past years, although several added a novel Latin American spice to this conference staple.

New research findings were fewer and farther between than ever, creating the sense that the meeting has evolved into a giant review paper rather than a place for colleagues to share their latest data. "This is more a world AIDS summit, where every 2 years we reexamine everything we know," said Julio Montaner, the new president of the International AIDS Society (IAS), the meeting's organizer.

Cohen was one of several presenters who stressed that the great gains in treatment have overshadowed prevention needs. Today, 3 million people in low- and middle-income countries receive anti-HIV drugs, but an estimated five people become infected for every two on treatment. "There has not been that push for prevention as there's been for treatment," said Peter Piot, head of the Joint United Nations Programme on HIV/AIDS. "If we thought the first phase was hard, we have to prepare for even tougher times."

Piot also noted that the characteristics of the epidemic keep changing in different locales, urging countries to "know their epidemics" and target prevention to the most vulnerable groups. In Thailand, where the

epidemic has been concentrated among injecting drug users and sex workers, married women now account for more new infections than any other group. In parts of sub-Saharan Africa, where epidemics have been primarily driven by heterosexual sex, injecting drug use is an increasingly important mode of spread. China, which has a large number of infected injecting drug users, today has a growing epidemic in men who have sex with men. In the United States, infections of whites peaked in the mid-1980s; blacks now account for 45% of the new infections and have an eight times higher risk of becoming infected, according to new estimates published by the U.S. Centers for Disease Control and Prevention (CDC). "The end of AIDS is nowhere in sight," said Piot.

The success with combinations of potent anti-HIV drugs, which reduce the amount of virus people carry and make them less infectious, has led to the increasing awareness that treatment is prevention, both for individuals and populations. But the degree to which the drugs can prevent infections has proved highly contentious.

A statement issued by the Swiss Federal Commission for HIV/AIDS in January on this topic served as a lightning rod. After reviewing the scientific literature, the Swiss commission concluded that a heterosexual person faced virtually no risk of becoming infected by having unprotected sex with an HIV-infected person on continued treatment, provided that person had undetectable levels of virus in the blood for 6 months and no sexually transmitted infections. The statement stopped short of explicitly discounting the value of condoms, but many thought that was its implicit message.

"There's condom absolutism, and everyone who questions it is put into controversy," said Bernard Hirschel, who heads the HIV/AIDS program at the University Hospital, Geneva. The main aims of the statement, he said, were to tell "discordant" couples--in which one is infected and the other isn't--who met these criteria that they could safely try to have children and also to combat a Swiss law that says an HIV-infected person who has sex without a condom can be held criminally liable, even in the absence of infecting a consenting partner.

Kevin De Cock, head of HIV/AIDS for the World Health Organization, and others blasted the statement as irresponsible. "It just doesn't seem like a cautious public health recommendation," said De Cock. "I don't think anyone's shown the threshold below which people cannot transmit."

A model published in the 26 July issue of *The Lancet* by David Wilson and colleagues at the University of New South Wales in Sydney, Australia, further emphasized the dangers. The study devised a mathematical model to compare 10,000 discordant couples that had unprotected sex for 10 years with the same number of couples who used condoms 80% of the time. The risk of transmission increased four times in the unprotected group because of occasional viral rebounds that happen to people on effective treatment.

Also hotly contested was the degree to which ongoing treatment can prevent transmission on the population scale. IAS President Montaner, a researcher at the University of British Columbia, co-authored an article in the 1 July issue of the *Canadian Medical Association Journal* that contends that potent treatment led to a decrease in HIV's spread in British Columbia. Specifically, their study notes that new HIV infections dropped about 50% in British Columbia from 1995 to 1998, the years when highly potent anti-HIV drugs first became available. During the same years, syphilis infections increased, suggesting that the drop

was not due to condom use or other behavioral changes. "Antiviral therapy greatly lowers infectiousness," contended Montaner.

But epidemiologist Geoffrey Garnett of Imperial College London countered that antiretroviral drugs are unlikely to make a large impact on transmission on a global scale. Roughly 80% of infected people do not even know their status. Of those who do, most are not eligible for free treatment until their immune systems have been substantially damaged--which means most transmissions occur long before people are taking the drugs.

Garnett and others encouraged their colleagues to embrace the notion of "combination prevention." No currently available intervention can by itself turn an epidemic around, but by combining treatment with preventive measures such as condoms and circumcision, it may be possible to create "a natural synergy," Garnett said. "Rather than arguing for a single magic bullet, we really need to be trying to focus everything that we can on what works to realize these natural synergies."

The growing enthusiasm for combination prevention in part reflects the dispiriting fact that the vast majority of biomedical prevention studies, from large human vaccine trials to **microbicides** to treatment of sexually transmitted diseases, have failed (see table). Still, many investigators have high hopes for what could be something of a magic bullet: pre-exposure prophylaxis (PrEP), which gives anti-HIV drugs to uninfected people. The idea is that people at high risk of infection will take the drugs shortly before having sex, much in the way that people take antimalarial drugs before visiting countries where that disease is prevalent. Studies around the world are now enrolling more than 18,000 people to test this concept--more than the number of people in AIDS vaccine trials, noted Mitchell Warren, head of the AIDS Vaccine Advocacy Coalition in New York City. UNC's Cohen predicted that PrEP, similar to the successful strategy used to prevent transmission of HIV from an infected, pregnant woman to her baby, "is almost certain to work."

The approach has had remarkable success in monkeys. Walid Heneine of CDC in Atlanta, Georgia, described experiments in which he and his colleagues inserted anti-HIV drugs into the vaginas of six monkeys and then 30 minutes later tried to infect the animals with vaginal infusions of an engineered AIDS virus. None of the animals became infected after 20 such "challenges," whereas seven of eight untreated control animals did.

Anthony Fauci, head of the U.S. National Institute of Allergy and Infectious Diseases in Bethesda, Maryland, said PrEP may lead to protection in more ways than one: The drugs prevent infections by killing or weakening the AIDS virus, which could trigger immune responses that subsequently derail infections. "That may be the first vaccine," said Fauci.

"Mexico conference considers pre-exposure prophylaxis for AIDS"

Date: 14 August 2008

Source: *BMJ*. 14 August 2008;News.

Author(s): Bob Roehr

http://www.bmj.com/cgi/content/extract/337/aug14_1/a1278?maxtoshow=&HITS=3&hits=3&RESULTFORMAT=&andorexacttitle=and&andorexacttitleabs=and&fulltext=microbicide%2C+microbicides&andorexactfulltext=or&searchid=1&usestrictdates=yes&resourcetype=HWCIT&ct

The possible use of a daily pre-exposure prophylactic pill against AIDS raised interest at last week's 17th international AIDS conference because of the recent failures of trials of vaccines and **microbicides**.

Several studies of pre-exposure prophylaxis are being launched in different parts of the world. Most involve a combination of two popular anti-HIV drugs, tenofovir and emtricitabine, in one pill, marketed as Truvada. The combination has amassed millions of people years of use. It seems to be safe, well tolerated, and holds the virus in check.

There are biological reasons to think that pre-exposure prophylaxis can work, and trials in monkeys are encouraging. But preventing infection is not the same thing as treating it, while not actually curing it. A single virus is thought to be enough to establish lifelong infection.

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

"Greater push to give women control over their sexual health"

Date: 11 August 2008

Source: *The Jamaica Observer*

Author(s): Ingrid Brown

http://www.jamaicaobserver.com/magazines/AllWoman/html/20080811T030000-0500_138928_OBS_GREATER_PUSH_TO_GIVE_WOMEN_CONTROL_OVER_THEIR_SEXUAL_HEALTH.asp

Jamaican-born Irene Jugasan, who was diagnosed with HIV in 1997, said had preventative measures been available for women, she would not have become infected.

She told All Woman that for 12 years she lived in abusive relationship with the father of her five children, who raped her repeatedly and refused to use a condom. She said while she would hide and take contraceptives to prevent further pregnancy, there was nothing she could do to protect herself against a sexually transmitted disease.

"I might not have been able to benefit from **microbicides** - in the case of HIV, a (topical) substance being developed to apply to condoms, for example, to prevent the virus - but I want to see it available on the market soon for all those women who are going through what I went through," she said.

She said when she pleaded for her spouse to use a condom, she was beaten, accused of cheating and was told that his Rastafarian religion did not encourage the "use of rubbers".

Irene, who has lived in the US since she was a teenager, said she would be the first to join any advocacy group in Jamaica which seeks to lobby the Government for **microbicides** to be made available at an affordable cost.

"Women must be given control over their lives because right now because I am sick, I cannot give the necessary care to my younger children and so I have not only given up my rights but that of my kids," she said.

Now, as statistics show that 70 to 90 per cent of all HIV infections in women are due to heterosexual intercourse and that women are twice as likely as their male partners to acquire HIV during sex, there has been a greater push for preventative measures that give women the control.

Currently, the focus has been on the development of vaginal and oral interventions which include the ability to take an antiretroviral tablet daily - an approach known as pre-prophylaxis (PrEP) or applying a vaginal **microbicide** gel also on a daily basis.

Specifically the trial will evaluate two ARV pills (tenofovir) and Truvada - drugs that are routinely used as part of combination therapy for treating HIV, and an ARV-based candidate **microbicide** called tenofovir gel.

As the number of trials are increasing around the world, Jamaicans are now being eyed as candidates for these ongoing **microbicide** trials.

Dr Zeda Rosenberg of the International Partnership for **Microbicides**, told All Woman here at the International AIDS Society (IAS) International AIDS Conference that they are in the early stage of discussions with research centres on the island.

She said the trial was not brought to Jamaica before because research centres were already doing great work on the HIV vaccine trials and so it would have been difficult for them to take on another trial.

"We also didn't want to get into turf issues," she said. However, since the vaccine trial did not yield the expected results, Rosenberg said it is an opportune time to introduce the **microbicides** trial to the island.

As for the HIV vaccine, Dr Seth Berkley, president of International AIDS Vaccine Initiative (IAVI), said "developing an AIDS vaccine may take more time and innovation than we might have once imagined, but we are confident that science will prevail".

Meanwhile, Dr Wayne Koff, senior vice-president of research and development at IAVI said "strong scientific evidence in both humans and animal models suggests that developing an AIDS vaccine is possible."

Rosenberg said before they approach the Jamaican government for permission, they want to ensure that the country has the scientist capacity to do this.

Once the approval is granted, Rosenberg said, they would then meet with all the relevant stakeholders. She said they are, however, less worried about not being able to get volunteers than they are about getting Government's approval.

Government bodies she said , will want to ensure the issue of safety for the population.

"And it is our responsibility to show them what we are doing and the safety of our products."

However, Dr Kevin Harvey, head of Jamaica's National HIV/STI programme said Jamaica would be willing to participate in such a trial.

"We would have to select our participants carefully and we must remember that no one will be infected by **microbicides**," he said.

He also made it clear that the vaccine trial never failed in Jamaica, but didn't get the required results on the international arena.

Meanwhile, Rosenberg said if the first set of **microbicide** trials which started in the 90s worked. They are hoping that the second generation trails which started in 2002, could be ready in the next two years.

"If current trials are successful, products could be ready in two to three years, if not five to eight years," she said. Rosenberg said **microbicides** will be an important prevention method for women as it would give them a powerful new way to protect their own health.

"If women are dying because of HIV they won't be here long enough to reach equality status and that is how **microbicides** fit in," she said.

Last year a local advocacy group, chaired by Dr Nesha Haniff,said it would be lobbying the Jamaican Government to make **microbicides** available to women free of cost once it has been licensed.

Citing violence against women as both a cause and consequence of HIV infection, Zonibel Woods of the Canada based Ford Foundation, in an address at the close of the AIDS conference here, highlighted the fear of violence from partners as a reason that some women do not seek treatment for HIV.

Woods said providing access to treatment cannot be divorced from ensuring a woman's right to live free from violence, and that attempts to scale up HIV treatment, while ignoring stigma and discrimination, will not work.

For real progress, the legal and policy environment to address violence against women must be strengthened along with the commitments to invest in, enforce, monitor and evaluate such policies.

Confronting gender-based violence is one of three priorities, presented in Wood's roadmap for responding to HIV in women.

She also outlined the importance of ensuring women's right to sexual and reproductive health, and investing in women's organisations so that women can participate effectively in decisions that affect their lives.

"Policies and budgets must support the full range of reproductive health services, including quality pregnancy and delivery care, and access to contraception," she said.

In addition, research and investment in technologies that put control of prevention in women's own hands also remain critical.

In closing, Woods welcomed the recent decision by the Global Fund to Fight AIDS, TB and Malaria to invest in gender transformative programmes. However, she emphasised that success in this regard depends on the engagement of women's organisations in setting in-country priorities, and the inclusion of experts in gender equality and women's empowerment funding on proposal review panels.

"Human rights at the core of AIDS control, conference told"

Date: 09 August 2008

Source: *Globe and Mail (Canada)*

Author(s): André Picard

<http://www.theglobeandmail.com/servlet/story/RTGAM.20080809.wxaims09/BNStory/specialScienceandHealth/home>

The AIDS epidemic has been with us for more than 25 years, and it will likely persist for at least 50 more, but by focusing on a "triple combination" of treatment, prevention and human rights, people living with HIV-AIDS will lead relatively normal lives, and health systems around the world will be strengthened, delegates to the International AIDS Conference heard yesterday.

"It is clear that we have moved on from the fruitless debate between prevention and treatment that has plagued us in the past," said Michel Kazatchkine, executive director of the Global Fund to Fight AIDS, TB and Malaria, arguing that they are complementary.

But he cautioned that wide-scale prevention, treatment and progress against the disease will not occur unless "human rights remain at the core of everything we do."

Mr. Justice Edwin Cameron of the Supreme Court of Appeal of South Africa told delegates that the growing criminalization of HIV-AIDS is a travesty that risks undermining progress and fuelling the epidemic.

Judge Cameron, who is HIV-positive himself, said that HIV-AIDS carries a mountainous burden of stigma and that no other illness is viewed with such fear and repugnance.

He noted that consensual same-sex activity is a criminal offence in 86 countries, including seven where it is punishable by death. In addition, a growing number of countries - including a dozen in Africa, the epicentre of the epidemic - have adopted laws making it a crime for the HIV-positive to have sexual relations, or even to be infected with HIV-AIDS.

"These laws are misdirected and bad. They are creating a crisis in HIV management and prevention efforts," Judge Cameron said.

More than 33 million people worldwide are infected with HIV-AIDS, including 2.7 million newly infected last year. Only three million people are being treated in the developing world, and for every two who begin

treatment, five people are newly infected.

The conference, which attracted some 22,000 delegates from 175 countries (including 888 from Canada), featured much discussion of how to scale-up access to drugs and on the promise of universal access to antiretroviral drugs by 2010.

Robert Fox, executive director of Oxfam Canada, excoriated United Nations officials for seemingly backing down on the goal of universal access.

"To say we are disappointed is an understatement. Has the AIDS Conference become just another expensive gab-fest?" he asked.

Julio Montaner, the new president of the International AIDS Society, acknowledged that the searches for an AIDS vaccine and for an effective **microbicide** have both stalled.

"But we must not despair," he said.

This is particularly true because antiretroviral drugs are proving so effective at keeping the disease in check.

But Dr. Montaner, director of the B.C. Centre for Excellence in HIV-AIDS, said it is not acceptable that only rich Westerners are benefiting.

"Let's be perfectly clear: Failure to enact a comprehensive, sustained and multipronged attack on the pandemic represents a crime against those infected, those affected and those susceptible. Indeed, it represents a crime against humanity," Dr. Montaner said.

Mark Harrington, executive director of the New York-based Treatment Action Group, said treating HIV-AIDS is a good investment because it strengthens health systems and improves access to health care.

"We are the vanguard of an unprecedented global citizens' movement for comprehensive universal primary health care for all," he said.

Mr. Harrington also warned that the AIDS fatigue that is setting in among governments, donors and activists could not only lead to a resurgence of the epidemic but to a dramatic worsening of health services across the developing world.

"In the time of AIDS, a nonstop crusader"

Date: 09 August 2008

Source: *The Washington Post*

Author(s): Manuel Roig-Franzia

<http://www.washingtonpost.com/wp-dyn/content/article/2008/08/08/AR2008080803914.html>

She drags colleagues out of bed for 5 a.m. runs in Hanoi and Bangkok. She touches down in Jamaica just long enough to deliver a wedding toast after stops in Washington and Atlanta. Once, she even quick-changed into a ball gown in the bathroom on the same day that she had flown from Washington to New York and back again for a soiree.

And now Helene Gayle, Global Poverty and AIDS Fighter, is trying to make small talk in a taxi lurching through the snarl of traffic here. "Nice weather," she says. "When does it get cold here?"

That conversational ground covered, Gayle is back inside her head. Deep inside. Her lips are pursed, emphasizing high cheekbones that would be the envy of any runway model. She's gazing into space, surely "processing something," as her brother Jacob Gayle says she tends to do, "multitasking more than any other human being could imagine." She's riffling through briefing papers for the 17th International AIDS Conference here. She's checking her BlackBerry for the fifth time in the past five minutes.

She has the reserved, socially cautious demeanor of the scientist who dwells in facts. And, as the head of CARE, she has to emote with passion and charisma to lead one of the world's largest charities, operating in 71 countries, with 13,000 employees and a \$545 million budget.

Somehow, they co-exist, these two Helene Gayles. The shy one and the one whom Bill Gates and his foundation once trusted with hundreds of millions of Microsoft-minted dollars, the one who kicks it in India with Richard Gere and talks shop with Bono. The one who makes the scene in designer gowns.

"She's an introverted loner," her brother says.

"She's a force of nature," says Aparajita Ramakrishnan of the Avahan India AIDS Initiative, a program launched by Gayle.

"A world-renowned woman -- it's so natural for her," U.S. Rep. Barbara Lee (D-Calif.) says.

A quarter-century after the emergence of AIDS, Gayle, 52, a pediatrician and epidemiologist by training, has cemented her place in an elite class of international decision makers who are shaping what the next quarter-century of the disease might look like. Theirs is a community of scientists, physicians and fundraisers who tend to slide back and forth from government gigs to charities to academia, just as Gayle has hopscotched from big jobs at the Centers for Disease Control and Prevention and the Gates Foundation to the helm of CARE.

Many in this interlacing world think Gayle will be shortlisted for something big -- secretary of health and human services or surgeon general -- if Barack Obama is elected president. Gayle, who has been donating money to Obama's campaigns since 2004, but also gave to Hillary Rodham Clinton's presidential campaign, said in an interview that she wouldn't rule out a return to government. CARE provided "in some ways my dream job," she says, but if a big government post were dangled in front of her, she'd "have to weigh that seriously."

For now, though, she inhabits a universe of disease chasers that has matured from the early, confused days of "the gay plague" -- a time when Gayle says activists sometimes threw tomatoes at her -- to a full-fledged global movement.

Once, they talked about a cure. They schemed about vaccines or therapies to vanquish the virus invading African villagers, Indian shopkeepers, Mexican prostitutes, Haitian beggars and American city dwellers. They got worked up about "**microbicides**," gels they hoped could protect against transmission. In their parlance, these were "technologies." But the virus is still spreading and the technologies, well, they haven't turned out as hoped. And still there is no cure.

So Gayle and a cadre of public health powerhouses are now more likely -- finally, some would say -- to talk about changing the way people behave, especially persuading them to have sex with fewer partners.

"It's unfortunate this wasn't recognized earlier," Helen Epstein, author of "The Invisible Cure: Africa, the West, and the Fight Against AIDS," says in an interview. "I was thrilled at the conference to see that Helene Gayle, who'd long supported a more technical approach, is coming around to the view that behavioral approaches are very good and have a lot of potential." Gayle was showcased at the Mexico City gathering - introduced as "one of the best known people at the conference" -- just days after the CDC announced that the U.S. HIV rate is much higher than previously reported. Like others here, she was in no mood to crow.

"Some of our hopes we'd placed in prevention technologies have had some setbacks," Gayle said onstage at a conference session. Later, she was characteristically matter-of-fact about what lies ahead:

"There's not going to be a vaccine tomorrow."

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

"Monkey study strengthens the case for a microbicide combining several anti-HIV drugs"

Date: 09 August 2008

Source: *AIDSmap.com News*

Author(s): Gus Cairns

<http://www.aidsmap.com/en/news/B24C79EE-D458-4417-BEBA-3564BA02B2E2.asp>

A study using a **microbicide** gel containing the antiretroviral drugs in the combination pill Truvada – tenofovir and FTC (emtricitabine) – completely protected six pigtail macaque monkeys from infection with a type of HIV designed to be infectious to monkeys, the XVII International AIDS Conference heard on Thursday.

This is a better result than seen in a previous study of a **microbicide** gel containing only tenofovir, which protected only two-thirds of monkeys from rectal infection (Cranage).

'Completely protected' means that six monkeys given twice-weekly rectal inoculations with three millilitres of a gel containing 5% FTC and 1% tenofovir, and then challenged 30 minutes later with a dose of 760,000 viral units of a laboratory-devised HIV called SHIV-SF162p3 were not infected after 20 doses. The reason five times as much FTC as tenofovir was used was simply because FTC is more soluble in water.

This dose, which is ten times the amount that should be expected to infected 50% of animals per inoculation, is actually a lower dose than that used in many previous studies, and was designed to mimic more closely the effects of regular sexual exposure in humans.

In contrast five out of six monkeys given the placebo gel (one each at weeks 2, 3, 4, 5 and 11) were infected. When asked why one monkey given placebo was not infected, presenter Walid Heneine said that such statistical outliers often happened, though the substance used to make the gel, hydroxyethylcellulose (HEC) has some antiviral effect too.

Two monkeys just given doses of the virus and no gel both became infected at weeks 3 and 4.

Low levels of both FTC and tenofovir were consistently detected in the blood of all the treated macaques 30 minutes after vaginal application of the gel: 67 nanograms (billionths of a gram) of FTC per millilitre (ng/ml) of FTC and 23 ng/ml of tenofovir. This is something like 2,000 times lower than the minimum dose of tenofovir required to inhibit 50% of HIV (its IC50). There have been considerable concerns that the absorption of **microbicides** into the blood might produce resistance in human subjects that were unwittingly HIV-positive or experiencing infection at the time; however Heneine commented that these drug levels were well below those necessary to create the selective pressure that results in drug resistance.

Heneine was asked whether the results of this study would put pressure on investigators conducting human trials of **microbicides** to start using combinations of drugs rather than single ones; at present all the ongoing and planned human trials are going to use single drugs, including one of tenofovir, CAPRISA, which started in May 2008.

Monkey studies of oral prophylaxis against HIV (pre-exposure prophylaxis: PrEP) have seen a similar pattern; a study showing that a single-drug regimen, also using tenofovir, produced partial protection (Subbarao) followed by a study showing that a tenofovir/FTC dual combination produced complete protection, albeit in this case against only 14 challenges with infectious virus. As a result of this, all but one of the current or planned efficacy studies of PrEP is using or has switched to drug combinations.

Heneine said that a decision would be taken on this question after an imminent study using tenofovir alone, under the same protocol of challenges and infectious dose, was completed by the CDC.

Reference

Parikh UM et al. Complete protection against repeated vaginal SHIV exposures in macaques by a combination emtricitabine and tenofovir topical gel. XVII International AIDS Conference, Mexico City, abstract THAC0503. 2008.

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2. PUBLISHED RESEARCH: MICROBICIDE-SPECIFIC

"Biomedical interventions to prevent HIV infection: evidence, challenges, and way forward"

Author(s): Padian NS, Buvé A, Balkus J, et al

Reference: Lancet. 16 August 2008;372(9638):585-99. Series, HIV Prevention.

<http://www.thelancet.com/journals/lancet/article/PIIS0140673608608855/fulltext>

Published Abstract: Intensive research efforts for more than two decades have not yet resulted in an HIV vaccine of even moderate effectiveness. However, some progress has been made with other biomedical interventions, albeit on the basis of inconsistent levels of evidence. The male condom, if used correctly and consistently, has been proven in observational studies to be very effective in blocking HIV transmission during sexual intercourse; and, in three randomised trials, male circumcision was protective against HIV acquisition among men. Treatment of sexually transmitted infections, a public health intervention in its own right, has had mixed results, depending in part on the epidemic context in which the approach was assessed. Finally, oral and topical antiretroviral compounds are being assessed for their role in reduction of HIV transmission during sexual intercourse. Research on biomedical interventions poses formidable challenges. Difficulties with product adherence and the possibility of sexual disinhibition are important concerns. Biomedical interventions will need to be part of an integrative package that includes biomedical, behavioural, and structural interventions. Assessment of such multicomponent approaches with moderate effects is difficult. Issues to be considered include the nature of control groups and the effect of adherence on the true effectiveness of the intervention.

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

"Identification of restriction endonuclease with potential ability to cleave the HSV-2 genome: inherent potential for biosynthetic versus "live" recombinant microbicides"

Author(s): Wayengera M, Kajumbula H, Byarugaba W

Reference: Theor Biol Med Model. 07 August 2008;5(1):18.

<http://highwire.stanford.edu/cgi/medline/pmid;18687114>

Published Abstract: BACKGROUND: Herpes Simplex virus types 1 and 2 are enveloped viruses with a linear dsDNA genome of ~120-200 kb. Genital infection with HSV-2 has been denoted as a major risk factor for acquisition and transmission of HIV-1. Developing biomedical strategies for HSV-2 prevention is thus a central strategy in reducing global HIV-1 prevalence. This paper details the protocol for the isolation of restriction endonucleases (REases) with potent activity against the HSV-2 genome and models two biomedical interventions for preventing HSV-2. Methods and results: Using the whole genome of HSV-2, 289 REases and the bioinformatics software Webcutter2; we searched for potential recognition sites by way of genome wide palindromics. REase application in HSV-2 biomedical therapy was modeled concomitantly. Of the 289 enzymes analyzed; 77(26.6%) had potential to cleave the HSV-2 genome in >100 but <400 sites; 69(23.9%) in >400 but <700 sites; and the 9(3.1%) enzymes: BmyI, Bsp1286I, Bst2UI,

BstNI, BstOI, EcoRII, Hgal, Mval, and Sdul cleaved in more than 700 sites. But for the 4: PacI, PmeI, SmaI, SmaI that had no sign of activity on HSV-2 genomic DNA, all 130(45%) other enzymes cleaved <100 times. In silico palindromics has a PPV of 99.5% for in situ REase activity (2) Two models detailing how the REase EcoRII may be applied in developing interventions against HSV-2 are presented: a nanoparticle for **microbicide** development and a "recombinant lactobacillus" expressing cell wall anchored receptor (truncated nectin-1) for HSV-2 plus EcoRII. CONCLUSION: Viral genome slicing by way of these bacterially- derived R-M enzymatic peptides may have therapeutic potential in HSV-2 infection; a cofactor for HIV-1 acquisition and transmission.

"1,2,6-tri-O-galloyl-beta-D-glucopyranose inhibits gp41-mediated HIV envelope fusion with target cell membrane"

Author(s): Sun W, Wang HT, Xia CL, et al

Reference: Nan Fang Yi Ke Da Xue Xue Bao. 01 July 2008;28(7):1127-31.

<http://highwire.stanford.edu/cgi/medline/pmid;18676243>

Published Abstract: OBJECTIVE: To observe the inhibitory effect of 1,2,6-Tri-O-galloyl-beta-D-glucopyranose (TGGP) from *Balanophora japonica* Makino on human immunodeficiency virus (HIV) entry into the host cells and explore the mechanisms. METHODS: TGGP was purified from *Balanophora japonica* Makino by n-hexane and ethyl acetate extraction and column chromatography. The inhibitory activity of TGGP on HIV gp41 six-helix bundle formation was measured with ELISA, N-PAGE and SE-HPLC, and the inhibitory effect of TGGP on HIV envelope glycoprotein-induced cell-cell fusion was detected using a non-infectious cell-based assay. RESULTS: TGGP inhibited HIV gp41 six-helix bundle formation, with an IC(50) of 1.37-/±0.19 microg/ml as determined by ELISA, and this activity was further confirmed by N-PAGE and SE-HPLC. TGGP at 25 microg/ml significantly inhibited syncytium formation between the effector (CHO-WT) and the target (MT-2) cells. CONCLUSION: The HIV transmembrane subunit gp41 mediates the entry of HIV into the target cells. TGGP can inhibit HIV fusion and entry into the target cells by inhibiting the formation of gp41 six-helix bundles, suggesting the potential of TGGP as a **microbicide** to prevent sexual transmission of HIV.

"An evaluation of intravaginal rings as a potential HIV prevention device in urban Kenya: behaviors and attitudes that might influence uptake within a high-risk population"

Author(s): Smith DJ, Wakasiaka S, Hoang TD, et al

Reference: J Womens Health (Larchmt). 01 July 2008;17(6):1025-34.

<http://highwire.stanford.edu/cgi/medline/pmid;18681822>

Published Abstract: PURPOSE: We sought to assess the potential acceptability of intravaginal rings (IVRs) as an HIV prevention method among at-risk women and men. METHODS: We conducted a

qualitative assessment of initial attitudes toward IVRs, current HIV prevention methods, and common behavioral practices among female sex workers (FSWs) and men who frequent FSWs in Mukuru, an urban slum community in Nairobi, Kenya. Nineteen women and 21 men took part in six focus group discussions. **RESULTS:** Most participants, both male and female, responded positively to the concept of an IVR as a device for delivering **microbicides**. Women particularly liked the convenience offered by its slow-release capacity. Some female respondents raised concerns about whether male customers would discover the ring and respond negatively, whereas others thought it unlikely that their clients would feel the ring. Focus groups conducted with male clients of FSWs suggested that many would be enthusiastic about women, and particularly sex workers, using a **microbicide** ring, but that women's fears about negative responses to covert use were well founded. Overall, this high-risk population of FSWs and male clients in Nairobi was very open to the IVR as a potential HIV prevention device. **CONCLUSION:** Themes that emerged from the focus groups highlight the importance of understanding attitudes toward IVRs as well as cultural practices that may impact IVR use in high-risk populations when pursuing clinical development of this potential HIV prevention device.

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3. PUBLISHED RESEARCH: RELEVANT BASIC AND TRANSLATIONAL SCIENCE

"Impact of mucosal inflammation on cervical human immunodeficiency virus (HIV-1)-specific CD8 T-cell responses in the female genital tract during chronic HIV infection"

Author(s): Gumbi PP, Nkwanyana NN, Bere A, et al

Reference: J Virol. 01 September 2008;82(17):8529-36.

<http://jvi.asm.org/cgi/content/abstract/82/17/8529?maxtoshow=&HITS=1&hits=1&RESULTFORMAT=&andorexacttitle=and&andorexacttitleabs=and&fulltext=microbicide%2C+microbicides&andorexactfulltext=or&searchid=1&usestrictdates=yes&resourcetype=HWCIT&ct>

Published Abstract: The female genital tract is the major route of heterosexual human immunodeficiency virus (HIV) acquisition and transmission. Here, we investigated whether HIV-specific CD8 T-cell-mediated immune responses could be detected in the genital mucosa of chronically HIV-infected women and whether these were associated with either local mucosal HIV shedding or local immune factors. We found that CD8+ T-cell gamma interferon responses to Gag were detectable at the cervix of HIV-infected women but that the magnitude of genital responses did not correlate with those similarly detected in blood. This indicates that ex vivo HIV responses in one compartment may not be predictive of those in the other. We found that increased genital tumor necrosis factor alpha (TNF-) and interleukin-10 (IL-10) levels correlated significantly with levels of Gag-specific CD8+ T cells at the cervix. Women who were detectably shedding virus in the genital tract had significantly increased cervical levels of TNF-, IL-1, IL-6, and IL-8 compared to women who were not detectably shedding virus. We were, however, unable to detect any association between the magnitude of cervical HIV-specific responses and mucosal HIV shedding. Our results support the hypothesis that proinflammatory cytokines in the female genital tract may promote HIV replication and

shedding. In addition, we further show that inflammatory cytokines are associated with increased levels of HIV-specific CD8 effector cells at the genital mucosa but that these were not able to control genital HIV shedding.

"The use of nonhuman primate models in HIV vaccine development"

Author(s): Morgan C, Marthas M, Miller C, et al

Reference: PLoS Med. 12 August 2008;5(8):e173.

<http://medicine.plosjournals.org/perlserv/?request=get-document&doi=10.1371/journal.pmed.0050173>

Published Abstract: In April 2006, the National Institute of Allergy and Infectious Disease (NIAID)-funded HIV Vaccine Trials Network and the NIAID Division of AIDS sponsored a workshop at which nonhuman primate (NHP) researchers and clinical trial scientists with HIV vaccine research expertise discussed how to more effectively use NHPs for evaluating HIV-1 vaccine candidates. This workshop precipitated a broad discussion on what types of NHP studies should be targeted in the critical preclinical pathway for HIV-1 vaccine candidates, especially those designed to elicit HIV-1-specific T cell responses. This paper describes the two-stage NHP screening strategy for T cell-based HIV-1 vaccines that emerged from discussions among the authors during the past year and a half. While conceived prior to the recent release of results for the phase IIB trial (STEP Study) of the Merck replication-incompetent adenovirus serotype 5 (Ad5)-HIV gag/pol/nef vaccine, we think the approach outlined below will be particularly useful for preclinical evaluation of vaccine candidates in the current vaccine pipeline for two reasons. First, the proposed strategy will eliminate suboptimal vaccine candidates early in the testing process (i.e., before initiation of phase I clinical trials). Second, the strategy would provide comparative immune response data in NHPs and humans for each promising HIV-1 vaccine product, information that could help the design of future vaccine candidates.

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

"HIV-1 transmission, by stage of infection"

Author(s): Hollingsworth TD, Anderson RM, Fraser C

Reference: J Infect Dis. 01 August 2008;198:687-93.

<http://www.journals.uchicago.edu/doi/abs/10.1086/590501>

Published Abstract: Background. The epidemiological impact of public health interventions targeted at reducing transmission of human immunodeficiency virus type 1 (HIV-1) during early or late-stage infection depends on the contribution of these disease stages to transmission within a particular epidemic. Methods.

Transmission hazards and durations of periods of high infectivity during primary, asymptomatic, and late-stage infection were estimated for HIV-1-serodiscordant heterosexual couples in Rakai, Uganda, by use of a robust probabilistic framework. Results. Primary infection and late-stage infection were estimated to be 26 and 7 times, respectively, more infectious than asymptomatic infection. High infectiousness during primary infection was estimated to last for 3 months after seroconversion, whereas high infectiousness during late-stage infection was estimated to be concentrated between 19 months and 10 months before death. Conclusions. Primary and late-stage HIV-1 infection are more infectious than previously estimated, but for shorter periods. In a homogeneous population, the asymptomatic stage of infection will typically contribute more to the net transmission of HIV-1 over the lifetime of an infected individual, because of its longer duration. The dependence of the relative contribution of infectious stages on patterns of sexual behavior and the phase of epidemics is discussed.

"Incidence of sexually transmitted infections among HIV-infected women using depot medroxyprogesterone acetate contraception"

Author(s): Overton ET, Shacham D, Singhatiraj E, et al

Reference: Contraception. 01 August 2008;78(2):125-30.

<http://www.ncbi.nlm.nih.gov/pubmed/18672113>

Published Abstract: BACKGROUND: Previous studies suggest that depot medroxyprogesterone acetate (DMPA) is associated with an increased risk of sexually transmitted infection (STI) acquisition. The primary aim of this study was to characterize the potential association between DMPA use and risk of STI acquisition among HIV-infected women. STUDY DESIGN: This is a retrospective cohort study among HIV-infected women followed at a university clinic from 1997 to 2005. Medical records were reviewed for demographic data, HIV parameters, self-reported condom use, substance use, duration of follow-up and incident cases of gonorrhea, chlamydial infection and trichomoniasis. RESULTS: Of 304 HIV-infected women identified, 82 received DMPA and 222 did not. Overall incidence rates of trichomoniasis, chlamydial infection and gonorrhea were 8.4, 4.0 and 3.1 cases per 100 person-years, respectively, with no significant differences between the women receiving or not receiving DMPA. CONCLUSIONS: In this HIV-infected cohort, STI rates were higher than the general population, yet DMPA use did not appear to enhance the risk of STI acquisition. This latter finding suggests that the concern for STI acquisition should not be a limiting factor in the use of DMPA in HIV-infected women. The implementation of additional secondary prevention strategies remains an important focus in the HIV epidemic.

"Relationship between levels of inflammatory cytokines in the genital tract and CD4+ cell counts in women with acute HIV-1 infection"

Author(s): Bebell LM, Passmore J, Williamson C, et al

Reference: J Infect Dis. 01 August 2008;198:710-14.

<http://www.journals.uchicago.edu/doi/abs/10.1086/590503>

Published Abstract: Inflammatory responses at mucosal surfaces after human immunodeficiency virus type 1 (HIV-1) transmission may influence disease outcome. We evaluated levels of interleukin (IL)-1, IL-6, tumor necrosis factor-, IL-8, IL-10, and IL-12 in genital tract and plasma specimens from 44 women with acute HIV infection and 29 HIV-negative control women (13 of whom were women in the acute HIV infection cohort who had preinfection samples available for analysis). Women with acute HIV infection had significantly elevated levels of IL-6, IL-10, and IL-12 in genital tract specimens and elevated levels of IL-1, IL-8, and IL-10 in plasma specimens, compared with HIV-negative control women. Levels of IL-1, IL-6, and IL-8 in cervicovaginal specimens from women with acute HIV infection showed a significant inverse correlation with systemic CD4+ cell counts, suggesting that mucosal inflammation is associated with low CD4+ cell counts during acute HIV infection.

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

"Intimate partner violence and HIV infection among married Indian women"

Author(s): Silverman JG, Decker MR, Saggurti N, et al

Reference: JAMA. 13 August 2008;300(6):703-710.

<http://jama.ama-assn.org/cgi/content/short/300/6/703>

Published Abstract: *Context* Despite reductions in prevalence of human immunodeficiency virus (HIV) infection among the general population of India, women account for a rising percentage of all HIV cases with husbands' risk behavior described as the major source of women's infection. Intimate partner violence (IPV) has been described as being associated with heterosexual transmission of HIV to women in India and elsewhere. *Objective* To assess the relationship between experiencing IPV and the occurrence of HIV infection in a nationally representative sample of married Indian women tested for HIV. *Design, Setting, and Participants* The Indian National Family Health Survey 3 was conducted across all Indian states in 2005 through 2006. The nationally representative sample included 124 385 married women; analyses conducted in 2007 and 2008 were limited to 28 139 married women who provided IPV data and HIV test results via systematic selection into respective subsamples. *Main Outcome Measures* Prevalence estimates of lifetime IPV and HIV infection were calculated and demographic differences assessed. Intimate partner violence was conceptualized as physical violence with or without sexual violence and then was further categorized as physical violence only vs physical and sexual violence. Regression models were used to estimate the odds ratios (ORs) and 95% confidence intervals (CIs) for HIV infection among Indian women based on experiences of IPV after adjusting for demographics and women's HIV risk behaviors. *Results* One-third of married Indian women (35.49%) reported experiencing physical IPV with or without sexual violence from their husbands; 7.68% reported both physical and sexual IPV, and 27.80% reported

experiencing physical IPV in the absence of sexual violence. Approximately 1 in 450 women (0.22%) tested positive for HIV. In adjusted models, married Indian women experiencing both physical and sexual violence from husbands demonstrated elevated HIV infection prevalence vs those not experiencing IPV (0.73% vs 0.19%; adjusted OR, 3.92; 95% CI, 1.41-10.94; P = .01). Physical IPV alone was not associated with risk of HIV infection. Women's personal sexual risk behaviors were not associated with HIV infection. *Conclusions*

Among married Indian women, physical violence combined with sexual violence from husbands was associated with an increased prevalence of HIV infection. Prevention of IPV may augment efforts to reduce the spread of HIV/AIDS.

"Determining optimal sample sizes for multi-stage randomized clinical trials using value of information methods"

Author(s): Willan A, Kowgier M

Reference: Clin Trials. 01 August 2008;5(4):289-300.

<http://ctj.sagepub.com/cgi/content/abstract/5/4/289>

Published Abstract: *Background* Traditional sample size calculations for randomized clinical trials depend on somewhat arbitrarily chosen factors, such as Type I and II errors. An effectiveness trial (otherwise known as a pragmatic trial or management trial) is essentially an effort to inform decision-making, i.e., should treatment be adopted over standard? Taking a societal perspective and using Bayesian decision theory, Willan and Pinto (Stat. Med. 2005; 24:1791-1806 and Stat. Med. 2006; 25:720) show how to determine the sample size that maximizes the expected net gain, i.e., the difference between the cost of doing the trial and the value of the information gained from the results. *Methods* These methods are extended to include multi-stage adaptive designs, with a solution given for a two-stage design. The methods are applied to two examples. *Results* As demonstrated by the two examples, substantial increases in the expected net gain (ENG) can be realized by using multi-stage adaptive designs based on expected value of information methods. In addition, the expected sample size and total cost may be reduced. *Limitations* Exact solutions have been provided for the two-stage design. Solutions for higher-order designs may prove to be prohibitively complex and approximate solutions may be required. *Conclusions* The use of multi-stage adaptive designs for randomized clinical trials based on expected value of sample information methods leads to substantial gains in the ENG and reductions in the expected sample size and total cost.

"Early participant attrition from clinical trials: role of trial design and logistics"

Author(s): Siddiqi A, Sikorskii A, Given CW, et al

Reference: Clin Trials. 01 August 2008;5(4):328-35.

<http://ctj.sagepub.com/cgi/content/abstract/5/4/328>

Published Abstract: *Background* Participant attrition from randomized controlled trials reduces the statistical power of the study and can potentially introduce bias. Early identification of potential causes of attrition can help reduce patient attrition. We performed secondary analyses of two trials involving cancer patients. *Purpose* To identify predictors of attrition during two early phases, i.e., from consent to screening (Phase-1), and from screening to intake interview (Phase-2) in two clinical trials. *Methods* Cancer patients undergoing chemotherapy were asked to enroll in one of two clinical trials. In each trial the benefits of a cognitive behavioral intervention were compared with a psycho-educational intervention to assist patients to manage cancer and treatment-related symptoms. Following consent patients were screened for their symptoms' severity to determine their eligibility. *Results* Of the 885 consenters 785 completed screening and of the 782 eligible for participation, 713 completed intake interview. In the first phase, longer delays between consent and first contact attempt, lower levels of patient education, minority race, and prolonged duration of screening increased the likelihood of dropping out with a significantly stronger effect on minorities than white patients. In the second phase, low education, being a minority, longer screening delays, and impact of symptom severity on enjoyment of life significantly increased probability of attrition. *Limitations* Participant reported causes of attrition were not modeled; however, exclusion of patients who died during the time period of this research meant that most patients leaving the study made a conscious decision to do so. *Conclusions* To assure preservation of external validity, the time between consent and randomization into the arms of a trial must be held to a minimum. Delays between contacts and run in time, that may include screening patients to assure they will benefit from a trial, must be balanced against rates of attrition. Compressing intervals between contacts is particularly important to retain minorities.

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5. EPIDEMIOLOGY

"War and poverty driving up HIV cases in Sudan"

Date: 10 August 2008

Source: *Associated Press*

<http://www.iht.com/articles/ap/2008/08/10/africa/AF-Sudan-HIV.php>

Poverty and the movement of war-displaced populations have driven the number of HIV/AIDS infections higher in Sudan, though a lack of data is preventing health officials from getting a full picture of the virus' spread, experts said Sunday.

Sudanese and United Nations AIDS experts told reporters in the capital, Khartoum, that an estimated 1.6 percent of Sudan's 37 million people were infected. But they cautioned that the real number was certainly higher and that better tracking would reveal that.

The increase in Sudan is contrary to a steady or declining trend among its African neighbors, such as Kenya.

In particular, the movement of large populations - those fleeing fighting in Darfur and those returning after the separate north-south conflict from areas with higher infection rates - were contributing to the spread. A peace deal in 2005 ended the 21-year conflict with rebels in the south but the war in the western region of Darfur continues and has claimed the lives of up to 300,000 people and displaced 2.5 million.

The number of infections based on the available data is thought to be between 350,000 and 600,000, and fewer than 2,000 patients are receiving regular treatment, the experts said.

Doctors and Sudanese officials speaking at a news conference said the 1.6 percent prevalence rate was surely underestimated because the data is outdated and based on surveys in a limited number of clinics, rather than a nationwide survey.

Abdel Kareem Gibreel Algoni, a Sudanese public health consultant who works in South Africa, said the spread of HIV is affected by poverty and illiteracy, both prevalent in Sudan.

"For Sudan practically now we are like in South Africa in the '90s," he said. "The virus is not that clever. We can overcome but it works on our ignorance, both political ignorance, economic ignorance and personal ignorance."

Algoni was among those who attended a U.N.-sponsored workshop in Khartoum for some 60 Sudanese physicians on the clinical management of HIV over the last three weeks.

According to the latest U.N. survey, selected regions in Sudan had between 1 percent and 3 percent infection rates. But Algoni said in his hometown of Abyei, south of Khartoum, some 18 percent of the population was seeking treatment for sexually transmitted infections at mobile clinics he privately set up. "Most probably, they will also have HIV."

Another physician at the workshop said doctors in hospitals in Khartoum and around it are reporting an average of three to five newly diagnosed HIV patients every day.

"We need to do something about it," said Zahir Babikr, who works as a specialist in infectious diseases in Manchester, England.

A nationwide survey has yet to be carried out, and conducting one without a reliable, updated census would be difficult, they said. A national survey expected this year has been delayed until next year because of a lack of funds.

A serious response to HIV/AIDS began only two years ago in Sudan and only recently did the country's religious leaders deem the use of condoms permissible, said Musa Bungudu, the head of UNAIDS Sudan. The use of contraceptives is not a universally accepted practice among Islamic scholars, most of whom oppose birth control.

Neighboring countries, such as Kenya and Uganda, have much higher rates of infection - 5 and 7 percent, respectively - but are showing signs of a decrease.

Sudan has the highest prevalence rate in the Middle East and North Africa and is the country where the virus is growing more widespread, beyond urban areas.

The U.N. AIDS program said the virus in Sudan is spread mainly through sex, not drug abuse. Stigma continues to make prevention and advocacy a challenge. Sudan has no national condom campaign, and HIV centers remain primarily in large hospitals in cities, inaccessible for most of the population.

Mohamed Abdel Hafeez, the manager for the National AIDS program, said that southern and eastern Sudan, as well as the capital, are believed to have the highest number of cases because of the return of large numbers of refugees from countries where HIV is more prevalent.

He said training for physicians and combatting the stigma associated with the disease, particularly among doctors, as well as resources to remote areas are all still lacking.

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6. HIV/AIDS VACCINES

"Elite" HIV wife may hold secret to AIDS vaccine"

Date: 12 August 2008

Source: *Reuters*

Author(s): Maggie Fox

http://news.yahoo.com/s/nm/20080812/hl_nm/aids_couple_dc

A woman who has never shown symptoms of infection with the AIDS virus may hold the secret to defeating the virus, U.S. researchers said on Tuesday.

Infected at least 10 years ago by her husband, the woman is able somehow to naturally control the deadly and incurable virus -- even though her husband must take cocktails of strong HIV drugs to control his.

She is a so-called "elite suppressor," and studies of her immune cells have begun to offer clues to how her body does it, the team at Johns Hopkins University in Baltimore said.

"This is the best evidence to date that elite suppressors can have fully pathogenic virus," said Dr. Joel Blankson, who led the study.

"The feeling was initially that they had defective virus," Blankson added in a telephone interview.

But the couple has been monogamous for at least 17 years, Blankson said, and tests show they are infected with the same strain of virus. What is different is the immune system of the wife, who cannot be

named for privacy reasons.

"That's a good sign in terms of developing a therapeutic vaccine," Blankson said. Such a vaccine would not prevent infection but might be used to treat patients.

The AIDS virus infects at least 33 million people globally and more than a million in the United States. It has killed 25 million people since it was identified in the early 1980s.

New figures show 56,000 people are infected every year in the United States, mostly gay and bisexual men but also injecting drug users and their sexual partners, both male and female, as well as newborns and recipients of contaminated blood transfusions.

Stalling Replication

Both the man and the woman, who are from Baltimore, were diagnosed 10 years ago, Blankson said. The husband is a former injecting drug user.

Tests showed that immune cells known as CD8 T-cells from the wife stalled HIV replication by as much as 90 percent, while the husband's T-cells stopped it by only 30 percent, Blankson's team reported in the *Journal of Virology*.

Her virus has also mutated in apparent response to this immune attack, becoming weaker, while her husband's virus has remained strong.

"Elite suppression offers clues to vaccine researchers on many fronts: how CD8 killer T-cells can attack HIV and how a stronger immune response can force HIV into a permanent defensive state," Blankson said.

"We are trying to figure out exactly how the T-cells work in her to inhibit viral replication," he added. "We are just trying to see what kind of cytokines they make."

Cytokines are immune system signaling proteins. One thing the researchers have noticed is that while the husband's T-cells make just one, called gamma interferon, hers made both that one and another called TNF, or tumor necrosis factor.

That cannot be the whole story, though, because AIDS researchers have tried using such immune system proteins in patients and they did not work well.

And her immune cells seem to make the response only when they encounter the virus.

Another clue: the woman may have unusual activity in her human leukocyte antigen system, or HLA, Blankson said. This important component of the immune system helps recognize antigens -- protein identifiers -- of enemies such as bacteria and viruses.

7. OTHER PREVENTION APPROACHES

"Circumcision protects against several sexually transmitted infections"

Date: 07 August 2008

Source: *Reuters*

Author(s): C Vidya Shankar

<http://www.medscape.com/viewarticle/578825?sssdmh=dm1.375139&src=nlconfnews&spon=1&uac=73804AZ>

Male circumcision has a protective effect against HIV, human papilloma virus and trichomonas vaginalis infections, researchers reported at the International AIDS Conference here.

Dr. Robert C. Bailey from the University of Illinois at Chicago and his team from Kenya reported 42-month follow-up results on the protective effects of male circumcision. They had previously reported encouraging results after 24 months of their randomized trial, which was stopped in December 2006 due to significant protective benefits, with the controls also being offered circumcision.

The cumulative incidence of HIV infection over 42 months among circumcised men was 2.6% as compared to 7.4% among controls, the researchers observed. The protective effect of circumcision was 64% (i.e., relative risk of infection, 0.36), they noted.

Male circumcision provides a sustained protective effect against HIV, Dr. Bailey's team concludes.

In another study, Dr. Bertran Auvert from Universite de Versailles, France and his team from South Africa analyzed the protective effect of male circumcision against other sexually transmitted infections.

In their randomized study of men aged between 18 and 24, the prevalence of human papilloma virus and trichomonas vaginalis was lower in the circumcised group with odds of 0.57 and 0.54, respectively, after 21 months follow up, they report. There was no effect on gonorrhoea rates.

"Circumcision could therefore be an indirect way of limiting the risk of genital cancers caused by HPV in women," Dr. Auvert said during a related press conference.

Male circumcision can prevent between 2 to 8 million new HIV infections in the sub-Saharan Africa, resulting in savings of around \$2 billion over the next 20 years, Dr. Auvert said.

Male circumcision is safe, with minimal side effects, and can be promoted as a universal preventive measure against HIV, Dr. Dirk Taljaard, one of the co-authors of the second study told Reuters Health.

"The studies of male circumcision have opened up a whole new era in the fight against AIDS: we now potentially have a new method of prevention," Professor Jean-Francois Delfraissy concluded during the press conference.

"The lady with the dildoes has plenty of Sister Love"

Date: 07 August 2008

Source: *The Body*

Author(s): Linda Villarosa

<http://www.thebody.com/content/conf/aids2008/art48138.html?mtrk=9612358>

In and around Atlanta, Dazon Dixon Diallo has been known as "the lady with the dildoes." That's because her organization, SisterLove Inc., hosts graphically entertaining Healthy Love parties to teach women the basics of HIV/AIDS prevention and safer sex practices while affirming their right to control their sexual health and have a little fun, too.

Diallo, 43, has also been known as "that woman who'll show you her cervix." Her group also sponsors Community PROMISE, a program that teaches women attending historically Black colleges and universities in Atlanta about sexually-transmitted infections, including HIV.

But these days, for several months a year the 20-year veteran of HIV education and community advocacy has a different gig: She's a farmer. In 2004, Diallo formed a partnership with three HIV/AIDS organizations and 66 community members affected by AIDS in South Africa to form the Thembuhlelo Trust Cooperative. Their collective, which owns 668 acres 90 miles east of Johannesburg, grows vegetables and raises chickens and cows. It provides food and hope for a rural area that's been devastated by both HIV/AIDS and poverty. The staff and volunteers of "the farm" also offer HIV education, counseling and testing between chasing chickens and managing their land. "When women are poor and economically dependent on men they are vulnerable to HIV," says Diallo, who presented a poster about her program at the XVII International AIDS Conference in Mexico City. She also participated in a satellite session on AIDS, Race, Gender and Inequality in the Americas on Tuesday.

"We realized that if we had even a little bitty piece of land and could feed some chickens and milk some cows, we could feed ourselves and sell whatever we don't need. We could give women and families living with HIV and affected by the disease empowerment and independence and help restore dignity and a sense of self."

Diallo's cutting-edge work -- on both continents -- illustrates both the similarities and differences of the global HIV/AIDS epidemic and its effect on women of African descent. According to the most recent UNAIDS report, worldwide, women account for half of all people living with HIV, and nearly 60 percent of HIV infections in sub-Saharan Africa. In South Africa, three out of every 20 citizens is infected with HIV, and disproportionately women.

In the United States, HIV prevalence in locations where African Americans are most heavily concentrated approaches those reported in South Africa and other greatly affected African countries. In both Africa and the United States, the overwhelming risk for women is unprotected sex with men.

Though SisterLove's approach is vastly different in Atlanta than it is in rural South Africa, Diallo points to the shared experiences. "We must address what we have in common as women of African descent," says

Diallo. "Women of African descent worldwide are bearing the brunt of the epidemic. Whether in Africa or in modern, post-feminist America we don't own our sexuality and in our relationships we defer to men. We act as if every woman who is positive has made a choice to have unsafe sex. But in reality, most of our decisions are really non-choices."

As in South Africa, at the heart of Diallo's work in the United States is the message that HIV prevention is a social justice and human rights issue. "I have a saying 'if you change women's lives, you change the epidemic,'" she says. "Women around the world are the backbone. Though we are the caregivers to our community, we have a voice we don't use. We have to get the power to women."

"Nevirapine persistence raises HIV resistance concerns"

Date: 05 August 2008

Source: *Reuters*

<http://www.medscape.com/viewarticle/578643?sssdmh=dm1.374799&src=nlconfnews&spon=1&uac=73804AZ>

Nevirapine persists in the blood and breast milk of HIV-infected mothers for at least 2 weeks after a dose of the drug has been given, which could lead to the development of viral drug resistance, according to study findings presented Tuesday at the International AIDS Conference in Mexico City.

Along with zidovudine (AZT), nevirapine has proven useful in developing countries in preventing vertical transmission of HIV, principal researcher Dr. David Katzenstein and colleagues, from Stanford University School of Medicine in California, note. However, once infection is established, the continued presence of the drug could promote resistance mutations.

"In the short term, nevirapine is better than nothing," Dr. Katzenstein said in a statement. "But in the long term, I'm concerned about conferring resistance. If you're talking about resistance on a broad scale, it could jeopardize future treatment for mothers and infants."

Prior research has suggested that maternal and neonatal treatment with nevirapine can cut HIV transmission by roughly half, resulting in a 13% risk of infection. However, there is evidence that up to 69% of HIV-positive mothers and 80% of infected infants will develop nevirapine-resistant strains.

The current findings are based on a study of 32 HIV-infected pregnant women in Zimbabwe.

The authors found evidence of nevirapine in the body for weeks after the drug had been given. Detectable blood levels of nevirapine were seen in over half of the women within 2 weeks of delivery. Moreover, at 2 weeks, the drug was found in the breast milk of two-thirds of women.

None of the women had drug-resistant HIV initially, but at 2 months, RNA testing revealed resistant strains in the blood of one third of women and in the breast milk of two-thirds.

Advanced disease, as indicated by lower CD4+ cell counts, was predictive of developing resistant strains, the authors note.

The investigators believe that one of the best ways to combat the drug resistance problem in developing countries is to improve access to combination therapies.

These findings reinforce "the need to treat these women with combination therapy, thereby providing better prevention for the infant, while providing better treatment for the mother," study co-author Dr. Seble Kassaye said in a statement. "Public health efforts should continue to expand combination therapy so that mothers and babies aren't left vulnerable to drug resistance."

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8. NON-HIV STIS AND REPRODUCTIVE HEALTH

"In Africa, hope for the stigmatized: Fertility clinics"

Date: 14 August 2008

Source: *The Washington Post*

Author(s): Stephanie McCrummen

<http://www.washingtonpost.com/wp-dyn/content/article/2008/08/13/AR2008081303771.html?wpisrc=newsletter>

In a country with one of the highest birthrates on Earth, where bearing children is considered a woman's singular purpose, Betty Apio leads an unusual life.

She has no children, not by choice, but because of a string of medical mishaps. Though she cares for nieces and nephews, she essentially lives on her own in the Kampala suburbs, where her living room is adorned with photos of the smiling husband who left her for a woman who could, as people here say, "produce." Some neighbors believe she is cursed. They shoo their children away from the pretty lady next door, a teacher who dreams of building a day-care center. She has learned to ignore them.

"People will never give you respect," said Apio, 44. "You have no value. People insult you -- 'You barren woman! You are useless!' It's horrible. And if you are not strong, you will not survive."

But Apio and an increasing number of other middle-class African women are seeking their social salvation in a service unheard of here until recently: fertility treatments. In the past few years, two clinics have opened in Kampala, one in Nairobi and a handful of others in major cities across the continent.

The clinics offer an alternative to superstitious explanations of infertility and the dubious advice of traditional healers, whose cures include having women run naked in circles around a dead sparrow at night. Fertility doctors are also bringing to light an uncomfortable truth about a condition almost always blamed on women: that at least half the time, the problem is with the man.

"The number of clients is going up by the day," said Annie Akatabaazi, who helps run a clinic that treats some of the few thousand women here who seek help each year. "Some ask to come at night, so they'll not be seen. Some call whispering. Sometimes they don't want to give you their name. They come saying, 'My husband is going to leave me if I don't have children.' And the men, once they find out, they come every day. If they have an appointment at 9 a.m., they show up at 8."

In much of Africa, the stigma of infertility is so severe that it often drives women -- and men -- to suicide. In some rural areas, women who die without children are carried in their coffins through the back door of the church. Women are sometimes branded witches and in other ways forced into isolation in a society that has few places for them.

The deeply entrenched culture of large families in Africa has to do with economics. In societies with virtually no government safety net, children represent financial security: One way or another, they are expected to provide for their parents when they get old. And for women in particular, children are a kind of insurance, protecting mothers against a divorce system that tends to grant property to men.

"In the African sense, children are an investment," said Robinah Kaitiritimba, a health-care advocate in Kampala, a bustling, hilly city of contrasts, where extreme poverty exists alongside malls and middle-class neighborhoods.

Women in Uganda, where polygamy is legal, have seven children on average; a recent newspaper article described in celebratory tones the life and times of a man who had 120 children with seven wives.

Though ideas about family are slowly changing, even relatively educated, middle-class women such as Apio suffer in a culture that seems designed to shun them.

She and her husband, who is also a teacher, married in the 1980s to the joy of both their families and with the absolute expectation that children would soon follow. They bought a house in Kampala, which Apio furnished with brown velour couches, tables with white doilies and their wedding photos. But the children never came.

Apio, who agreed to discuss her situation in the hope that other women would feel less alone, attributes her condition to an abortion she had when she was young. Getting pregnant at her age was taboo in her village, she said, and so was discussing the matter with her mother. So Apio's sister arranged for her to have an abortion at a hospital.

Abortion is illegal in Uganda, and Apio's procedure was, she learned later, botched.

After she and her husband were unable to conceive, she went to a gynecologist who told her that one of her fallopian tubes was blocked. He recommended an operation to fix it. When Apio awoke, the doctor told her that he had removed the tube.

Distraught, she went to another doctor, who also recommended an operation. He removed the functioning tube, though she still does not know why.

Her husband's family taunted her and told him to find another woman, which he eventually did. They had two children. When Apio refused to pay school fees for them, his relatives complained she was jealous. "They say to my husband, 'Why are you keeping that woman?' " she said.

His new wife does not allow the children to visit Apio, saying she "has a dark heart," she said. Her husband comes around a couple of times a week, or sometimes just once a month. Though he mostly annoys her, Apio said she is worried that he will leave and take the house from her. So she tries to be kind.

"Sometimes I want a divorce and to stay on my own," she said. "Then I go to my mother, and she says to stay, that I'll shame the family. She says to stay in the marriage, even if it's painful. But sometimes I want to leave -- to do my own things. Sometimes I get annoyed with him and tell him not to come back. But then he comes back. I worry about the future."

Adoption is rare among Africans, though many care for the children of less-fortunate relatives.

Women unable to conceive often end up supporting the children of their sisters and brothers, aunts and uncles. Apio has put a nephew through college and is putting two nieces through private school, though she realizes she will not be able to depend on them later in life.

"When the time comes, they'll go," Apio said, noting that the nephew never comes around anymore.

She has found some comfort from her sister and two brothers and some relief at a counseling center in Kampala called Joyce. Its founder, Ritah Sembuyu, named the center for the child she never had. She runs support groups that comfort women by offering them scientific explanations of their situations, camaraderie and referrals to fertility clinics.

"Even if people tease me now, I don't care," said Apio, who is holding out hope that in vitro fertilization might work in her case.

Prakesh Patel, who runs one of the fertility clinics in Kampala, said women often pretend to be going to this shop or that, before rushing through his doors. Many come without their husband's knowledge. They offer to pay for late-night appointments. And they often wind up crying in his office. "I say to them, 'This is not a disease. There are many like you -- you don't have to be ashamed,' " Patel said.

Then he contends with the physical and psychological trauma done by traditional healers, who often prescribe herbs that do more damage than good. He gives basic anatomy lessons. He tells women they do not have to tolerate their obnoxious relatives and at times encourages women to consider their childlessness a blessing -- a way to escape the confines of a male-dominated society.

"I tell them that if people pressure you, don't let them," he said. "Women here are considered property -- as objects rather than human beings. Like a table with one leg gone wobbly is a useless table, if a woman cannot produce, she is a useless woman."

9. POLITICS AND POLICY

"Know your epidemic, know your response': a useful approach, if we get it right"

Author(s): Wilson D, Halperin DT

Reference: Lancet. 09 August 2008;372(9637):423-26. Comment.

<http://www.thelancet.com/journals/lancet/article/PIIS0140673608608831/fulltext>

Published Abstract: Led by UNAIDS, Know your epidemic, know your response has become a rallying cry for an intensified focus on HIV prevention, spurred by the sobering realisation that for every person enrolled on antiretroviral treatment, many more become newly infected.¹ The quest to better understand epidemics reflects growing recognition that there is no single global HIV epidemic, but rather a multitude of diverse epidemics. No single prescription can apply to countries as diverse as South Africa, Egypt, Russia, Thailand, or Papua New Guinea. The era of standard global prevention guidance is over.

However, there is a globally useful distinction between concentrated and generalised epidemics, which are fundamentally different—not because of arbitrary prevalence thresholds, but about who gets infected and how. Epidemics are concentrated if transmission occurs largely in defined vulnerable groups—typically sex workers, men who have sex with men, and injecting drug users, and their sexual partners—and if protecting them would protect wider society. Conversely, epidemics are generalised if transmission is sustained by sexual behaviour in the general population and would persist despite effective programmes for vulnerable groups. For too long, the global HIV-prevention community has pursued generalised responses in concentrated epidemics, concentrated approaches in generalised epidemics, or hedged their bets and done a bit of everything.^{2–7}

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

"Putting prevention at the forefront of HIV/AIDS"

Author(s): Horton R, Das P

Reference: Lancet. 09 August 2008;372(9637):421-22. Comment.

<http://www.thelancet.com/journals/lancet/article/PIIS014067360860882X/fulltext>

Published Abstract: From the very beginning of the global response to the AIDS pandemic, prevention has been marginalised. Treatment has dominated. This systematic imbalance in clinical and public-health programmes is largely responsible for the fact that around 2.5 million people become newly infected with HIV each year. The publication of a Series by The Lancet on the state of the science of HIV

prevention—together with a call for action by leading academics, UNAIDS, and the World Bank—signifies a new commitment to stop the virus and its consequences.^{1–6}

When one surveys the political hinterland of this pandemic, one immediately discovers a litany of declarations and commitments, leaders' forums and high-level consultations.¹ With what result, one might reasonably ask, given the still appalling toll that HIV wreaks? It may be right that WHO calls the finding that nearly 3 million people are now receiving antiretroviral therapy “a remarkable achievement”.⁷ But it is surely scandalous that this access to medicines campaign has not been matched by an access to prevention campaign. The 3-by-5 initiative is symbolic of a striking international imbalance and inequity in our response to HIV/AIDS.

For the truth is that this pandemic will never be defeated without effective prevention. To be sure, no single prevention strategy will be sufficient. We need combined prevention, including a portfolio of biomedical, behavioural, and structural interventions.^{2–4} We must increase the health-systems strengthening element to our policy and practice. We must continue to argue for more funding. We need to rethink our approach to evaluating prevention. And we must find better ways to enhance coordination between international and national actors.

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

"Making those who transmit HIV into criminals doesn't protect people from the virus - Cameron"

Date: 08 August 2008

Source: *Health-e*

Author(s): Kerry Cullinan

<http://www.health-e.org.za/news/article.php?uid=20032047&PHPSESSID=e2f9abdec49ccbd02384d5cb3495b66>

A homeless man in Texas has been sentenced to 35 years in prison for harassing a public servant with a deadly weapon.

His weapon? His own saliva, which he spat at the police officer who was trying to arrest him for drunken behaviour. It was deemed “deadly” because the man has HIV.

In Zimbabwe, an HIV positive 26-year-old woman was sentenced to a suspended term of five years' imprisonment for having unprotected sex with her lover.

She was convicted of “deliberately infecting another person” -- but her lover tested HIV negative and didn't want to proceed with the charges.

These cases were part of a world-wide “rash phenomenon” where law-makers were enacting new laws “that create special crimes of HIV transmission or exposure”, Judge Edwin Cameron told the plenary of the 17th International AIDS Conference on Friday (8 Aug).

“At least a dozen” African countries have adopted laws that criminalise HIV transmission, he said.

“AIDS is now a medically manageable condition. It is a virus, not a crime, and we must reject interventions that suggest otherwise.

“Criminalisation is warranted only in cases where someone sets out, well knowing he has HIV, to infect another person, and achieves this aim,” argued Cameron.

In general, the laws would not protect people from HIV: “In the majority of cases, the virus spreads when two people have consensual sex, neither of them knowing that one has HIV. That will continue to happen, no matter what criminal laws are enacted,” said Cameron.

“Criminalisation places blame on one person instead of responsibility on two,” said Cameron.

But the vast majority of people knew how HIV was transmitted and everyone in the position to choose their sexual partners needed to take responsibility for safe sex.

“No one suggests that a person knowing he has HIV, who sets out intending to infect another, and achieves his aim, ought to escape prosecution (such deliberately stabbing someone with an injecting needle containing blood with HIV). He has set out deliberately to harm another and he has achieved his purpose as surely as if he had wounded his victim with a firearm or a knife.

“But in cases where there is no deliberate intention, the categories and distinctions of the criminal law become fuzzy and incapable of offering clear guidance,” said Cameron.

He said that the most painful thing for people like him, who were living with HIV, was that criminalisation increased the stigma of AIDS.

“No other infectious disease is viewed with as much fear and repugnance as HIV is. Because of this, stigma lies at the heart of the experience of every person living with or at risk HIV.”

Cameron appealed to the conference to condemn the criminalisation of HIV transmission as there was “no public health rationale for invoking criminal law sanctions against those who unintentionally transmit HIV or expose others to it”.

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10. HIV/AIDS FUNDING

"HHS Secretary Leavitt to visit HIV/AIDS projects in Cote d'Ivoire"

Date: 12 August 2008

Source: *Kaiser Daily HIV/AIDS Report*

http://www.kaisernetwork.org/daily_reports/rep_index.cfm?DR_ID=53902

HHS Secretary Mike Leavitt on Wednesday is scheduled to arrive in Cote d'Ivoire, where he will visit projects aimed at fighting HIV/AIDS, malaria and other diseases, AFP/Google.com reports. Leavitt will spend two days in the country, which receives funding from the President's Emergency Plan for AIDS Relief. PEPFAR has allocated \$120 million for Cote d'Ivoire's HIV/AIDS efforts from April 2008 to March 2009, according to the U.S. embassy in Abidjan. The \$120 million represents a 43% increase in funding compared with the previous year, AFP/Google.com reports. According to the embassy, a second five-year HIV/AIDS project likely will be approved by the government this year (AFP/Google.com, 8/11).

CDC Director Julie Gerberding and coordinator of the President's Malaria Initiative Tim Ziemer are traveling with Leavitt, and they also will visit Ethiopia and Mali. The officials will meet with government representatives in the three countries; visit hospitals, research centers and clinics; and travel to rural communities. They also will meet with religious leaders and look at the role of faith-based organizations in health care (HHS release, 8/8).

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11. ANNOUNCEMENTS

Annual Clinical Trial Safety Reports Proposed by FDA

<http://www.fda.gov/OHRMS/DOCKETS/98fr/FDA-2008-D-0386-gdl.pdf>

Clinical trial sponsors would be asked to submit annual development safety update reports (DSURs) under a guideline proposed by the FDA to match one issued previously by the International Conference on Harmonisation (ICH).

The reports would replace those used now to ensure the safety of drugs in clinical trials, such as the IND Annual Report.

In a DSUR, sponsors are supposed to update the trial's status, summarize their understanding and management of identified and potential risks, describe new safety concerns that could affect the protection of trial subjects and examine whether the information collected during the previous year fits with knowledge about the product's safety, the draft says.

While the DSUR should focus on data from interventional trials, sponsors are advised to include other findings that affect subject safety, according to the draft. Those findings may come from nonclinical studies, related clinical trials conducted by the sponsor's development partners and noninterventional or compassionate-use studies.

Some of the information expected in a DSUR — based on safety findings, serious adverse reactions and relevant published articles — may be provided in the sponsor's periodic safety updates for marketed products involved in current clinical trials, the draft says.

The draft can be viewed at www.fda.gov/OHRMS/DOCKETS/98fr/FDA-2008-D-0386-gdl.pdf. Comments are due Oct. 6.

FDA Guidances Track ICH Guidelines on Clinical Trial Reporting, Pharmacopeia

<http://www.fda.gov/OHRMS/DOCKETS/98fr/FDA-2008-D-0386-gdl.pdf>

The FDA has issued five draft guidances to bring the agency into compliance with the International Conference on Harmonisation (ICH).

The lengthiest of the guidances is an ICH guideline from June on development safety update reports proposed as the common standard for annual clinical trial safety reporting among the ICH regions instead of existing reports such as the IND Annual Report in the U.S. and the EU Annual Safety Report.

“This comprehensive, thoughtful annual review can provide an additional level of assurance of protection for subjects in clinical trials,” the guideline says. “In addition, by harmonizing the format, content and timing of annual safety reports, regulators in the three ICH regions can receive the same information at the same time, thereby reducing the number of reports generated.” The draft can be viewed at the above website.

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