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The Seattle Treatment Education Project's (STEP) EZINE is an electronic treatment resource newsletter distributed monthly to case managers, front-line workers, people affected by HIV/AIDS, physicians, other public health and allied health professionals and people living with HIV/AIDS.

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Novel agents show promise as anti-HIV compounds

By Megan Rauscher
Published by www.natap.org

NEW YORK (Reuters Health) - Compounds called pyridine oxide derivatives not only have the ability to inhibit HIV replication in a test tube, they also interfere with viral gene expression [which genes the virus "turns on" or "turns off"—ed.], according to the latest research from a team that has been studying these novel compounds.

It may be possible that these new agents could control the ability of HIV to reproduce in both early and later stages of the illness, and may even make the virus enter a dormant state, Dr. Jan Balzarini, Dr. Miguel Stevens, and others from the Rega Institute for Medical Research in Leuven, Belgium suggest

Previously, Dr. Balzarini found that several pyridine oxide derivatives selectively target HIV-1 reverse transcriptase (RT), acting much like the non-nucleoside reverse transcriptase inhibitors (NNRTIs) [e.g., AZT 3TC, D4T, among others--ed]. "This target is operative before the incorporation of the viral genome in the host cell chromosomes [in other words, before the genetic make-up of the virus inserts itself into the genetic make-up of the cell it infects.—ed]," the doctor said.

"But several [other] members of this group of compounds have clearly an inhibitory effect against HIV at a target in the replication cycle of the virus that is operational after the virus is incorporated in the host cell chromosomes," she continued.

These compounds inhibit both HIV-1 and HIV-2 RT and are the focus of the team's latest work, published in the medical journal Antimicrobial Agents and Chemotherapy.

In contrast to the pyridine oxides that inhibit just HIV-1, those that inhibit both HIV-1 and HIV-2 possess a novel dual mode of anti-HIV action independent from HIV RT inhibition, Dr. Balzarini and colleagues report.

"Time-of-addition experiments revealed that these pyridine oxide derivatives interact at a post-integration step in the replication cycle of HIV," they write. "The compounds interfere with the transcription process ...and may have the potential to prevent reactivation of the virus, which is an interesting added value for the compounds," Dr. Balzarini said. [These compounds seem to act at the same place as do other NRTIs as well as at a place farther along in the reproduction of the virus—ed.]

"This unique feature, as well as the wealth of chemical modifications that may be introduced into this series of molecules, makes this class of compounds of potential interest as a new lead in the development of candidate drugs for anti-HIV chemotherapy," the researchers write.

SOURCE: Antimicrobial Agents and Chemotherapy, October 2003.

What *are* MRSA and VRE?

Edited by the STEP staff

Staphylococcus aureus is a common type of bacteria (germ) that is often found in the nose, but can also grow in wounds and other sites of the body, where the infection may cause great harm. Methicillin is an antibiotic or medication that is used to treat these infections. In the early days of antibiotic therapy, Penicillin was used to treat staph infections, but gradually the organism became resistant to most antibiotics except for methicillin. Over time, the bacteria have become resistant to methicillin as well, so this antibiotic is no longer able to kill the germ. If a person has an infection with this germ that cannot be treated with methicillin, the person is said to have *Methicillin-resistant Staphylococcus aureus*, or **MRSA**, and must be treated with other antibiotics.

Enterococci are bacteria that are normally found in the bowel and vagina of humans. When they get outside these areas, these bacteria can cause infections of the urinary tract, wounds, or bloodstream. Vancomycin is an antibiotic that usually works to treat these infections. Infections caused by Enterococci that are resistant to Vancomycin are called *Vancomycin-resistant Enterococci*, or **VRE**, and are very difficult to treat.

What conditions increase the risk of acquiring these organisms?

People may be carriers or infected with these germs. Carriers means that the germ is present in or on the body but is not causing illness. Infection means that the germ is present and is causing illness. Signs of illness can include fever, elevated white blood cell count, pus, pneumonia, and inflammation (warmth, redness, swelling).

In general, healthy people are at low risk of getting sick with MRSA or VRE. Risk factors for infection include history of using antibiotics; underlying diseases or conditions such as chronic renal (kidney) disease, insulin-dependent diabetes mellitus, peripheral vascular disease, and dermatitis or skin lesions; invasive procedures such as dialysis; presence of invasive devices such as urinary catheters; past hospitalization and long hospital stays; history of having a drug-resistant bacterium; and older age.

How are these germs spread from one person to another?

MRSA is transmitted primarily by contact with a person who has an infection or is a carrier of the bacteria. The germ can be spread by direct contact with the person or by the hands of someone caring for the person touching others before washing hands. MRSA can survive for an hour or more on environmental surfaces such as floors, sinks, blood pressure cuffs, etc. but these are ***NOT*** the most likely source of spread.

VRE can be spread person-to-person by the hands of personnel or indirectly on contaminated environmental surfaces and patient care equipment. Studies have found that VRE can live for a long time on hands, gloves and

environmental surfaces. For example, the germ has been found after 5-7 days on countertops, 24 hours on bedrails, and 60 minutes on telephone handpieces.

What can be done to prevent the spread, especially in home care settings?

Patients that are carriers or infected with drug-resistant organisms who are discharged to their homes require no special control measures beyond regularly cleaning all surfaces contaminated by secretions or touched by hands. They should be allowed to socialize and participate in normal activities as long as draining wounds are covered, bodily fluids are contained, and good hygiene is practiced. Patients should tell anyone caring for them that they are carriers or infected with a drug-resistant germ.

Handwashing is the most important way to prevent the spread. The risk of spreading the germ depends on the site of the infection in the patient and the type of contact each person has with the patient. Therefore, each person should take the appropriate precautions for the type of contact. For example, those with casual contact may simply wash their hands after the visit, while persons who expect to have contact with body fluids should wear disposable gloves. Hands should be washed after removing the gloves.

Family members and visitors should wash their hands after direct contact with the patient or with items the patient has touched and before leaving the home. Hands should be washed with soap and water for a minimum of 10 seconds. Everyone should wash hands after using the toilet, before preparing food and before eating.

Healthcare providers and workers that are providing care in the home of an infected person should follow the recommended practices and precautions. They should focus on preventing spread to others via the clinical bag, clothing, and medical or other equipment that is carried to and from the home by healthcare personnel. Reusable equipment must be cleaned either in the patient's home or bagged prior to leaving the person’s home. Hands should be thoroughly washed before leaving.

Those living with HIV/AIDS are at greater risk. Good hand-washing techniques and the use of gloves (barrier precautions) are keys to prevention and control. Hands should be washed before and after every contact with the infected person

Cleaning: Linens should be changed and washed on a routine basis and any time they are soiled. Towels used for drying hands after contact should be used only once. Dishes should be washed in hot water and dried. The patient's environment should be cleaned on a routine basis and any time it is soiled with body fluids.

Soap and Water: A WEAPON AGAINST HIV?

Edited by Janice Price

[Editor’s note: Soap and water will no doubt prove useful as a tool to reduce HIV transmission in developing countries where condoms are unavailable or negotiation for condom use is impossible. Soap and water is no substitute for proven safer sex methods such as male or female condom use. By reporting this story, STEP is in no way advocating reliance on soap and water to prevent HIV infection. In addition, the diaphragm is not considered an effective barrier to HIV. STEP warmly encourages its readers to use condoms.]

Soap and water may prove to be a very effective weapon again HIV. A recent study demonstrated that a bar of soap and tap water mixture decreased HIV viral activation by 30-fold. When soap and water was mixed with washings

from a woman's cervix and vagina (CVL) and with seminal fluid (SL) [cum], there was a 57% to 87% decrease in the number of viable peripheral blood mononuclear cells (a type of white blood cell that carries HIV).
"The present study demonstrates that soap and water solutions should be effective in inactivating HIV and HIV-infecting cells associated with barrier contraceptives (*e.g.*, diaphragms and female condoms) or cells that are present in the vaginal canal," the researchers conclude.

Dr. Jay A. Levy, coauthor of the report, [said] that "the main message of this research is that regular soap works to kill HIV. Its major use in this regard should be on other instruments, such as diaphragms, used to prevent HIV transmission." Levy emphasized that soap and water should not be used as a douche to eliminate HIV from the vagina. First, this method has not been tested, he stressed. Second, soap can have adverse effects, including disrupting the lining of vagina that might actually make it more susceptible to infection, and altering the normal population of vaginal microbes that can protect against other infections.

STUDY REPORT

Postcoital [after the sex act] genital cleansing with soap and water may be effective in preventing HIV infection, but the direct effect of a soap solution on HIV has not been reported before the results of this study were released. HIV can be inactivated by a variety of chemicals and surfactants as well as by an antimicrobial hand wash product. However, these agents may be irritating to the genital mucosa and difficult to obtain. This report documents the effects of common soap and water on HIV as well as white blood cells, which may also play a key role in HIV transmission.

A commercial bar soap (Ivory) was completely dissolved in warm tap water at several concentrations. For these studies, a diluted solution was used (1 g/1,000 ml) to ascertain possible conditions in the environment.
The direct virus-killing action of genital secretions was first measured. Suspensions of virus were then evaluated for infectivity after exposure to an equal volume of soap and tap water, tap water alone, or control medium for 2 to 6 minutes.

When HIV was exposed to control medium, CVL alone, SF alone, or a CVL-SF mixture, no noticeable effect on viral infectivity was noted until the 6 hour time point, when a tenfold decreased infectivity of the virus in CVL was observed. By 12 hours, the CVL had caused a 1,000-fold decrease in virus infectivity. In contrast, HIV in control medium or CVL-SF did not show a tenfold decreased infectivity until 12 hours after incubation, and at 24 hours a 1,000-fold dilution of virus still resulted in a productive infection.

Exposure of HIV to soap and water for 2 to 6 minutes decreased viral infectivity by more than 1,000-fold. When the virus was in a CVL-SF mixture, the virucidal activity of the 1-g/1,000 ml soap and water mixture was completely eliminated. However, with a 1-g/200 ml soap solution, viral infection was reduced by more than 30-fold after either 2 or 6 min of exposure.

In addition to the widespread use of soap solutions to clean female barrier contraceptives after their removal from the vaginal canal, several recent studies have indicated that the practice of vaginal cleansing with soap, detergents, or disinfectants is common in the developing world. The present study demonstrates that soap and water solutions should be effective in inactivating HIV and HIV-infected cells associated with barrier contraceptives or cells that are present in the vaginal canal. For these experiments, Ivory bar soap was chosen because of its relatively simple ingredients and its accessibility to women internationally. However, soap and water needs to be further evaluated for its effects on the vaginal [bacteria] if used as a douche in conjunction with female barrier contraceptives. In addition, in developing countries, access to clean water is imperative for these simple approaches to be effective in preventing HIV transmission.

The information in this article was modified from the original study report. For access to the entire study, including methods, please note the following citation: **Virucidal Efficacy of Soap and Water against HIV in Genital**

Secretions Antimicrobial Agents and Chemotherapy, Oct 2003, p. 3321-3322, Vol. 47, No. 10. Jonathan Z. Li, Elizabeth C. Mack, and Jay A. Levy

More on Oral Sex and the Risk of HIV Transmission

In the following two articles we will entertain two different views on oral sex transmission of the HIV virus

AIDSClinical Care, December 2003
By G. Sonia Nagy, MD
Published by *www.natap.org*

Detailed interviews of a cohort of gay men with acute infection provide further evidence that oral sex can be a route of HIV transmission and suggest that penile piercings may increase this risk.

Although the risk for HIV transmission through oral sex is difficult to determine (in large part because the mode of transmission in any given case can be difficult to establish), published studies suggest that the risk associated with fellatio is low, **but not zero.**

For more information see AIDS 1998; 12:2095-105; 7th Conference on Retroviruses and Opportunistic Infections, Abstract 473; and AIDS 2000; 16:2350-2352).

Investigators in Sydney conducted detailed interviews with 75 HIV acutely infected gay men between 1993 and 1999 to assess all risk behavior in the 6 months preceding seroconversion and to determine the likely mode of transmission.

The researchers established the most likely mode of transmission by sorting exposures according to a risk hierarchy: high risk (sharing needles for intravenous drug use, unprotected receptive and insertive anal intercourse), medium-to-low risk (condom-protected receptive and insertive anal intercourse, blood or semen contact with an open wound, oral sex, and penile-anal external contact without insertion), and no risk (visits to dentists, blood donation in Australia, stepping on a discarded syringe, sex with a verified HIV-negative partner, and mosquito bites).

Each exposure was also adjusted for the likelihood that the partner was infected, the partner's likely viral load, the timing of the contact, relative to seroconversion illness, the presence of skin lesions or breakdown in either partner, duration of the exposure, and occurrence of ejaculation.

HIV transmission was thought to have occurred from high-risk behaviors in 60 men and from low-to-medium risk behaviors in 15 men. Eleven of the men with low-to-medium risk behaviors reported condom-protected anal intercourse, and several noted that they assumed this practice was completely safe. In five cases, the likely source of transmission was concluded to be oral sexual contact. Three of these five men, all of whom had also engaged in protected anal sex, had penile piercings (none of which had been performed recently), and the oral sex involved insertive fellatio. In the fourth case, the infected individual reported no anal intercourse, but receptive oral sex with ejaculation in the setting of Gingivitis and open wounds in the mouth from dental treatment. In the fifth case, an infected individual reported a single instance of condom-protected receptive anal intercourse with a man who was having anal sex for the first time, and a recent history of multiple oral sexual contacts with casual partners.

This is a retrospective, small case series that cannot definitively establish either a route of transmission or the likelihood of transmission per oral sexual act. Questionnaires and interviews are flawed in that recall of past exposures may be inaccurate. However, the methodology employed in this case series was thorough and, in some instances, uncovered risk behaviors that were not initially reported. The link between possible breaches in skin integrity from piercings and the transmission of HIV needs to be further investigated.

Dr. Nagy is Assistant Professor of Medicine at Mount Sinai School of Medicine in New York.

Richters J et al. HIV transmission among gay men through oral sex and other uncommon routes: Case series of HIV seroconverters, Sydney. AIDS 2003 Oct 17; 17:2269-71.

HIV transmission among gay men through oral sex and other uncommon routes: case series of HIV seroconverters, Sydney

Special Proteins Provide Possible Explanation Why Oral Transmission of HIV is Uncommon

By Janice Price

{[Editor's note: Uncommon does not mean zero. Oral transmission of HIV is a documented phenomenon.]

Oral transmission rates of HIV are low, as indicated by data indicating that over 90% of HIV infections occur across other mucosal surfaces. But the reason for this was obscure until results of a study looked at some special proteins present in the cells that line the mouth became available. The proteins are called human biodefensins. Normally, these are expressed by certain cells only during the inflammatory process, but the cells of the mouth lining make these proteins under normal conditions. Human biodefensins –2 and –3 (but not –1) appear to inhibit the formation of the CXCR4 receptor on the cell surface, thus removing a port of cell entry for HIV. Interestingly, these biodefensins do not inhibit the formation of the CCR5 receptors, which are another port of entry for HIV. This may explain why most oral HIV transmissions are of a form of the virus that prefers the CCR5 portal rather than CXCR4.

If you wish to read the entire journal article, please note the following citation:. Quinones-Mateu, M., *et. al.* Human epithelial b-defensins 2 and 3 inhibit HIV-1 replication, AIDS 2003, vol. 17, no. 16. *F-39-F48.*

New AIDS Clinical Trials Unit study opens

ACTG Study 5142

A study to compare the effectiveness of three regimens for the initial treatment of HIV Infection

The study will examine the use of a lopinavir/ritonavir (a ritonavir-enhanced, second generation protease inhibitor)-based regimen, a non-nucleoside reverse transcriptase inhibitor (NNRTI)-based regimen, and a nucleoside-sparing regimen as the first treatment of HIV-1 infection.

Eligibility:

- HIV positive
- Planning to start anti-HIV treatment
- No prior antiretroviral therapy
- 18 years old or older, men and non-pregnant women
- HIV RNA (viral load) of 2,000 copies or above

The study will last for about three years.

Exams and lab tests provided at no cost. Only TDF, EFV, LPV/r, and d4tXR will be provided by the study.
Subjects receive $20 per study visit.

Contact Alyssa or Lori at the ACTU 206.731.3184

Trials at Swedish Medical Center

1. Tipranavir Early Access Program. There are limited openings in this program. Please contact Healther Algren at (206) 386-2820

2. Protease Inhibitor Study. You may be eligible to join a research study of a medication for HIV disease if you have taken HIV medications in the past that no longer work for you and you are currently taking a combination of HIV medications and your viral load is over 1,000 copies. Please contact Janice Price at (206) 386-2523.

What's new at Lifelong AIDS Alliance?

Destiny "Destino" Williams joins the Lifelong Case Management team as the new bilingual Spanish speaking case manager starting January 2004. Destiny joins us from having recently work at the 45th Street Clinic as a member of the front desk and pharmacy teams. Destiny has spent time in Guatemala and El Salvador interviewing families to document their family history. Destiny has great respect and passion for helping the Latino Community and our Seattle community in general.

We also would like to encourage the community to visit the new and remodeled Transgender Center at the Seneca building. Miss Rickey Snowden, the new Transgender Program Coordinator will welcome you with open arms and will be ready to answer any questions you may have.

Miss Rickey Snowden was born and raised in Las Vegas, Nevada and moved to Seattle in 1980 and came to terms with her identity 4 years ago while attending a transgender support group. Miss Rickey Snowden goal as the Transgender Program Coordinator at Lifelong AIDS Alliance is to bring the transgender community together.

She said- "I like to be a role model for transgenders across all races and here at Lifelong, we are going to provide a safe place where every transgender will be welcome to speak openly about their sexuality, HIV/AIDS issues as well as how to prevent this disease"
The transgender program will held support groups 3 times a week. The regular hours are Monday thru Friday 9am to 1pm. **There is an Open House today, December 30th from 7pm 'til 9pm at the Transgender Center**. For more information, call Miss Rickey Snowden at 957-1742

ACKNOWLEDGEMENTS

- Please note that this is not a complete list of all HIV-related treatment information. STEP strives to provide the very latest in HIV/AIDS treatment information, research and drug development information. The most current research directions and antiretroviral drug data are provided throughout the Ezine publications. You will find highlight reports as well as extensive follow-up reports from many of the AIDS research and science conferences on the Ezine. In addition, all STEP quarterly treatment journals are available on our Web site at http://www.thebody.com/step/steppage.html or by calling our National Talkline at 1-888-399-STEP (7837). STEP works hard to give unbiased treatment information to all interested parties. If you have comments, questions, suggestions or grievances, please contact step@lifelongaidsalliance.org. Special thanks to the following for contributing written material or editing this publication

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