STEP Electronic treatment Ezine

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By Adimika Meadows, Senior Treatment Educator, adimikam@stepproject.org

The Seattle Treatment Education Project's (STEP) EZINE is an electronic treatment resource distributed bi-monthly to people living with HIV/AIDS, people affected by HIV/AIDS, case managers, front-line workers, physicians, other public health and allied health professionals. STEP's contact information is: Seattle Treatment Education Project, 1123 East John Street, Seattle, WA 98102, (206) 329-4857 or 1-877-597-STEP (WA, OR, AK, HA, ID, MT)

WOMEN'S HEALTH

Diaphragm and Microbicide Combination may work to block HIV

Researchers suggest that a diaphragm's protectiveness of the cervix and upper reproductive tract, which are vulnerable to HIV infection, may be an effective HIV prevention method when combined with a microbicide. "Widespread violence against women, double standards of sexual behavior, and the imbalance of power in many sexual partnerships make methods initiated and controlled by women critically important," researchers note. This may be a route for women to control sexual practices and safety during sex acts.

This study concludes that the cervix is a very vulnerable area to infection, possibly more than the surface of the vagina. The top layer of cells covering the cervix is thinner and more fragile, allowing them to be subject to crumbling, than that of the vagina, and the cervix is the location that receptors required for HIV infection are concentrated. Additionally, a cervical barrier can prevent virus particles from being transported into the fallopian tubes and peritoneal cavity by uterine contractions.

Although no one knows whether the diaphragm in conjunction with a microbicide is as effective as a condom in preventing HIV transmission, this report suggests new options for researchers to begin asking the question.

SOURCE: AIDS 2001;15:1595-1602.

HPV Infection, Cervical Disease Prevalent in HIV-Infected Women on HAART

High-risk human papillomavirus infections and squamous intraepithelial lesions persist in many HIV-infected women despite highly active antiretroviral therapy (HAART), researchers report in the *Journal of Infectious Diseases* in September.

A study looked at the effect of HAART on high-risk human papillomavirus infections and related cervical lesions by prospectively evaluating virologic and cytologic markers of HPV infection in 163 HIV-infected women. Twenty-seven of the women were untreated, 62 were being treated with reverse transcriptase inhibitors, and 74 were being treated with HAART. The researchers report that 65% of the 163 women had evidence of HPV infection at baseline. Treatment with HAART seemed to have no demonstrable effect on the persistence of high risk HPV or evolution of lesions.

After adjustment for gynecologic therapy, the only variable significantly associated with the persistence of HPV infection was a CD4 cell count <350 cells/µL. Only HAART-treated subjects experienced a significant increase in CD4 cell counts over an average follow-up period of 15.4 months ($p < 0.001$).

The results seemed to indicate that HPV cervical infection and related disease persist in a high proportion of women receiving HAART, particularly those with the longest history of HIV infection (long-term survivors), and suggest that, regardless of antiretroviral regimen and its effect on HIV replication, the number of CD4 cells remains a strong marker for survival.

The study found a significant reduction in the incidence of new HPV-16 and HPV-18 infections in women treated with HAART, compared with untreated and reverse transcriptase-treated women ($p = 0.043$). "This may suggest that the immune recovery induced by HAART can (in patients with higher CD4 cell counts) duplicate that found in the general population (i.e., early treatment results in regression of acute HPV infections at higher risk for evolution but in less effect on well-established or advanced HPV disease)", states the authors.

The recommendation eluded from this article indicates that all HIV-infected women should be routinely monitored for the emergence of high-grade cervical lesions and cervical cancer.

SOURCE: J Infect Dis 2001;184:547-551

ANTIVIRAL THERAPY

Dual Therapy (2 Drug Combo) May Work for Some HIV Patients

Findings published in the Journal of Antimicrobial Chemotherapy, suggest that patients with viral loads below 10,000 copies per milliliter of blood and at least 300 to 350 CD4+ cells per microliter of blood can be treated effectively with dual NRTI (Nucleoside Reverse Transcriptase Inhibitor) therapy. The therapy "seems to ensure a stable virological, immunological and clinical disease evolution after at least 2 years of follow-up," explains the journal article.

This study suggests that one in five HIV-infected patients appear to remain stable on treatment with an older form of antiretroviral therapy and could be spared the toxicity of highly active antiretroviral therapy (HAART). Common side effects of HAART therapy can include liver damage, abnormal body fat deposits and diabetes. The older treatment, known as dual therapy is not recommended by the Department of Health and Human Services and the Henry J. Kaiser Family Foundation's **Guidelines for the Use of Antiretroviral Agents in HIV-Infected Adults and Adolescents**. HAART still remains the current gold standard of treatment for HIV therapy.

The study followed 163 HIV-infected patients for an average of 24 months after they began dual-NRTI treatment. To monitor HIV patients, viral load and CD4 count were monitored. Over the course of the study period, 113 (or 69%) of the patients on dual-NRTI therapy had viral loads that remained below stable levels. Viral loads climbed above stable levels in the remaining 50 patients, but only 32 (19.6%) saw their CD4 cell count fall by more than 20%. None of the patients in the study developed AIDS or died during the study period.

SOURCE: Journal of Antimicrobial Chemotherapy 2001;48:299-302.

New Guidelines for the Management of Occupational Exposures to HBV, HCV, and HIV and Recommendations for Post exposure Prophylaxis

The U.S. Public Health Service (PHS) has published previous guidelines for the management of HIV exposures that included considerations for post exposure prophylaxis (PEP). The last version was dated in 1998. Since publication of the 1998 HIV exposure guidelines, several new antiretroviral agents have been approved by the Food and Drug Administration (FDA) and more information is available about the use and safety of HIV PEP. In addition, questions still exist regarding considerations about PEP regimens (when the source person's virus is known or suspected to be resistant to one or more of the antiretroviral agents that might be used for PEP).

This revised report updates and consolidates all previous U.S. Public Health Service recommendations for the management of health-care personnel who have occupational exposure to blood and other body fluids that might contain hepatitis B virus (HBV), hepatitis C virus (HCV), or human immunodeficiency virus (HIV). New recommendations for HIV PEP include a basic 4-week regimen of two drugs (zidovudine [ZDV] and lamivudine [3TC]; 3TC and stavudine [d4T]; or didanosine [ddI] and d4T) for most HIV exposures and an expanded regimen that includes the addition of a third drug for HIV exposures that pose an increased risk for transmission. When the source person's virus is known or suspected to be resistant to one or more of the drugs considered for the PEP regimen, the selection of drugs to which the source person's virus is unlikely to be resistant is recommended.

In addition, this report outlines several special circumstances (e.g., delayed exposure report, unknown source person, pregnancy in the exposed person, resistance of the source virus to antiretroviral agents, or toxicity of the PEP regimen) when consultation with local experts and/or the National Clinicians' Post-Exposure Prophylaxis Hotline ([PEPline] 1-888-448-4911) is advised. The report still indicates that occupational exposures should be considered urgent medical concerns to ensure timely post exposure management and administration of HBIG, hepatitis B vaccine, and/or HIV PEP.

There has been public concern also has arisen about the use of PEP when it is not warranted. Data in the new revisions may indicate that some health-care personnel take a full course of HIV PEP after exposures that do not confer an HIV transmission risk. The new guidelines for PEP were published in the MMWR (Morbidity and Mortality Weekly Report) in

the June 29, 2001/volume 50/No. RR-11. If you have any questions in regards to the new guidelines, you may call the STEP Talkline at 1-877-597-STEP or see the new guidelines at:
http://www.cdc.gov/mmwr/PDF/RR/RR5011.pdf

The appendices of the report include:

- APPENDIX A. Practice Recommendations for Health-Care Facilities Implementing the U.S. Public Health Service Guidelines for Management of Occupational Exposures to Bloodborne Pathogens
  http://www.cdc.gov/mmwr/PDF/RR/RR5011.pdf
- APPENDIX B. Management of Occupational Blood Exposures
  http://www.cdc.gov/mmwr/PDF/RR/RR5011.pdf
- APPENDIX C. Basic and Expanded HIV Post exposure Prophylaxis Regimens
  http://www.cdc.gov/mmwr/PDF/RR/RR5011.pdf

The Federal Drug Administration (FDA) Announces two important Meetings of interest in HIV

On October 3-4, 2001, the Federal Drug Administration (FDA) Advisory Committee will have a public meeting located in Silver Springs, Maryland. On October 3, 2001, the committee will discuss new drug application (NDA) 21-356, for Viread, otherwise known as tenofovir disoproxil fumarate (300mg) tablets, proposed for the treatment of human immunodeficiency virus (HIV) infection, sponsored by Gilead Sciences, Inc. Viread is currently available to patients through the Expanded Access Program. For more information on Viread, call the STEP Talkline at 1-877-597-STEP or contact Gilead Sciences website at: http://www.gilead.com/webpage_templates/frame_home.php3

On October 4, 2001, the FDA Advisory committee will discuss another new drug applications (NDA) 21-266, for Vfend (voriconazole) tablets, and (NDA) 21-267, Vfend I.V. (voriconazole) for Infusion, sponsored by Pfizer Global Research and Development, and proposed for the treatment of invasive aspergillosis, serious Candida infections, infections caused by Scedosporium spp. and Fusarium spp., and rare and refractory infections. For more information on either Vfend for Infusion or Vfend, contact the STEP Talkline at 1-877-597-STEP or the Pfizer Global Research and Development website at: http://www.pfizer.com/cr/groton/welcome.html

HEPATITIS/HIV CO-INFECTION

FDA APPROVES NEW LABELING FOR PEG-INTRON FOR USE WITH REBETOL

Hepatitis C infection is responsible for 8,000 to 10,000 deaths per year in the United States, according to the Centers for Disease Control and Prevention (CDC). The virus is spread mainly through contact with the blood of an infected person. About 85% of people infected with the hepatitis C virus (HCV) become chronically infected, meaning the virus stays in the blood and liver, multiplies, and may slowly attack the organ over a period of decades.

The majority of people infected with HCV do not develop severe liver disease and some may not need treatment. Most studies report that cirrhosis (advanced liver scarring) develops in 10 percent to 20 percent of people with chronic HCV infection over a period of 20 to 30 years. Liver cancer develops in 1 percent to 5 percent.

The combination of PEG-Intron and Rebetol is a new treatment option for patients with chronic hepatitis C. Although treatments come with the risk of serious side-effects, many individuals with chronic HCV infection can benefit from those treatments. The FDA has approved a supplemental biologics application for PEG-Intron (peginterferon alfa-2b), an injectable product approved to treat patients with chronic hepatitis C infections, to be used in combination with REBETOL capsules (ribavirin).

PEG-Intron is a longer acting form of interferon than Intron A, (a previously approved form of interferon), and requires only one injection per week for one year compared to three per week for Intron A. In January 2001, the FDA approved PEG-Intron alone to treat chronic hepatitis C in patients with liver disease who had not been treated before with interferon alpha and who are at least 18 years old. In the past, the FDA has approved various interferons including Intron A (interferon alfa-2b) to treat chronic hepatitis C as well as the combination of Intron A and Rebetol. This approval was based on

studies indicating a better patient response to the combination than with Intron A alone. All three products -- PEG-Intron, Intron A and Rebetol -- are manufactured by the Schering Corporation.

PEG-Intron with Rebetol was somewhat more effective than Intron A with Rebetol. Twenty-four weeks after treatment ended, 52% of patients who received the PEG-Intron combination had undetectable HCV virus levels in the blood compared to 46% for the Intron A combination. In patients with genotype 1 virus (a particularly difficult to treat variant of the HCV virus), the difference in sustained responses was 41% compared to 33%.

PEG-Intron with Rebetol caused the same types of adverse events as Intron A/Rebetol, although more adverse events were reported. Adverse events reported in the clinical trials included flu-like symptoms, psychiatric disorders (including depression), and decreases in red blood cells, (which deliver oxygen to the body), white blood cells (which help fight infection), and platelets (which help stop bleeding). Patients taking either combination treatment must be carefully monitored by their physicians and get regular blood tests to check for side-effects and to see if the treatment is working.

A Medication Guide for patients will accompany each prescription of PEG-Intron to explain the adverse events associated with its use as well as how to most effectively use the product. You can get more information by calling the STEP Talkline at: 1-877-597-STEP or visiting these websites:
http://www.ndhnow.com/pt_takingpeginterferonalfa2bpegintron.htm
http://www.hepatitisinnovations.com/pro/pegintron/product_info.html and
http://www.centerwatch.com/patient/drugs/dru697.html

SOURCE: Federal Drug Administration and Schering Companies

NEW DIAGNOSTIC TESTING MEASURES

FDA APPROVES FIRST NUCLEIC ACID TEST (NAT) SYSTEMS TO SCREEN PLASMA FOR HUMAN IMMUNODEFICIENCY VIRUS (HIV) AND HEPATITIS C VIRUS (HCV)

The Food and Drug Administration has licensed the first nucleic acid test (NAT) systems intended for screening of plasma donors. These test systems are expected to further ensure the safety of plasma-derived products by permitting earlier detection of HIV and HCV infections in donors.

Although effective procedures for virus inactivation are required in the manufacturing of all U.S. licensed plasma derivatives, removal of potentially infectious donations through donor screening adds a safeguard by limiting the amount of virus contamination that the manufacturing process must clear.

NAT is a recently developed technology that allows detection of very small amounts of genetic material (DNA or RNA) by a process of massive copying (amplification) of a gene fragment. The approved test systems permit highly sensitive detection of RNA from HIV-1 and HCV in test pools of 512 plasma samples obtained from multiple donors. Currently, donors of blood and plasma are tested for antibodies to HCV, antibodies to HIV, and HIV-1 antigens, which are the virus' own proteins. However, there is still a "window period" during which a donor can be infected, but have negative screening tests. With the use of NAT for HCV, the "window period" for detection of HCV is reduced by 57 days (from an average of 82 days to 25 days). For HIV-1, the average window period with antibody tests is 22 days. Antigen testing cuts the window period to approximately 16 days and NAT further reduces this period to 12 days.

Since 1997, FDA and other government research agencies has encouraged the investigation of NAT technology through the use of experimental protocols, in the hope of improving the safety of plasma derivatives and further reducing the risk of an infectious unit of blood being transfused. For more information, please call the STEP Talkline at 1-877-597-STEP or look at these related websites: http://www.alphather.com/ or http://www.ngi.com/

SOURCE: National Genetics Institute, Alpha Therapeutic Corporation and the FDA

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 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 website at http://www.thebody.com/step/steppage.html or by calling our TALKLINE at 1-877-597-STEP. STEP works hard to give unbiased treatment information to all interested parties. If you have comments, questions, suggestions or grievances, please contact adimikam@stepproject.org or ezine@stepproject.org.

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