



STEP Electronic treatment Ezine

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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)

TREATMENT GUIDELINES

STEP has a continued commitment to providing the latest treatment guidelines and treatment information. In the past few months, several people have requested the updated or revised guidelines for HIV infection. Here are links to these important resources:

Use of Antiretroviral Agents in HIV-Infected Adults and Adolescents

An update from the April 2001 version of the guidelines and all revisions, this version covers such areas of HIV treatment as considerations for initiating therapy in asymptomatic patients and new cautions regarding interruptions of therapy (so-called drug holidays). Also among the updates, the combination of didanosine and lamivudine has been added to the "Strongly Recommended" category.

Use of Antiretroviral Agents in Pediatric HIV Infection

The guidelines address the pediatric-specific issues associated with antiretroviral treatment and provide guidance to health care providers caring for infected infants, children, and adolescents. Sections that have been updated include Treatment Recommendations, Choice of Initial Antiretroviral Therapy, Available Antiretroviral Drugs, and the Appendix on Characteristics of Available Antiretroviral Drugs.

For the updated version of both guidelines, please go to: <http://hivatis.org/trtgdlns.html> or the National AETC Resource Center at <http://aids-ed.org>. Revisions are highlighted on the Web versions.

If you have any questions in regard to the new guidelines, you may call the STEP Talkline at 1-877-597-STEP.

INTERNATIONAL HIV TREATMENT ISSUES

Boehringer-Ingelheim Works to Make Nevirapine Available to Prevent Mother-to-Child Transmission of HIV

The debate around pharmaceutical companies providing antiretroviral medications for Third World countries at low cost has stirred great interest in the HIV policy and advocacy arena. It has allowed examination of what programs are available that provide seriously affected countries with the necessary medications to treat AIDS or related opportunistic infections. Last year, Boehringer-Ingelheim provided its drug, Viramune, free of charge to countries for use in preventing vertical transmission of HIV (infection of HIV from pregnant mothers to their children).

In the past, when only AZT was shown to be effective in vertical transmission in the United States, African advocates had to argue to reduce the costs of anti-HIV drugs for access in Africa. In the past few years, researchers have found other options in addition to AZT. For example, nevirapine, given as a single dose to a mother at the onset of labor and a single dose to

the infant within 72 hours, can help reduce vertical transmission for about \$4 a dose. Although research studies have highlighted that a single tablet of Viramune can significantly reduce the risk of transmission to a child, the South African government seems concerned about the effectiveness of nevirapine and the possibilities of women developing resistances to the drug. According to a recent Boston Globe article, fewer than 18,900 African babies have received Viramune since the beginning of the program. This may be due to the lack of support from the African governments.

South Africa's Treatment Action Campaign (TAC) and other international advocacy groups were frustrated that the South African government was hesitating to follow the example of Brazil or of non-governmental organizations that are taking the initiative to import generic drugs to provide access to affordable treatment for HIV/AIDS. In South Africa recently, AIDS activists sued the government for not importing nevirapine or other antivirals for treatment of HIV. The United Nations Special Session on HIV/AIDS in June allowed participating countries to set global targets and timetables on issues reflecting the importance in the HIV/AIDS epidemic. Included in the key goals of the "Global Response to Crisis" is the 20 percent reduction in the number of children born with HIV by the year 2005.

One of the major issues that Boehringer-Ingelheim seems to have faced with its program in Africa is that of working only with African governments instead of working with African communities. The "lack of HIV/AIDS counselors in clinics; insufficient numbers of testing kits to test HIV-positive expectant mothers; a lack of attention toward educating women in Africa; and, in many countries, a lack of political will to push costly AIDS programs" may be additional problems as reported in a recent Boston Globe article. The requirements for the drug access program include accessibility of HIV testing kits and counselors to administer the HIV test to expectant mothers, distribution of nevirapine information, and demonstration that the anti-HIV medicines will be given to those patients who need them. Boehringer has set up an application process that is open both to governments and to private nonprofit organizations that run maternity programs within countries. The program has seen recent success in the Democratic Republic of Congo, Rwanda, Senegal, Uganda, Zambia, and Zimbabwe in Africa, and Guyana in the Caribbean.

Statistics provided from IAVI and UNAIDS. The UNAIDS Web site is unaids.org/ and UNAIDS can be reached at: unaids@unaids.org. For additional updates on AIDS access in Africa, consult the Web sites <http://www.tac.org.za/> and <http://www.globaltreatmentaccess.org/>.

Sources:

United Nations, "Global Crisis/Global Action", United Nations Special Session on HIV/AIDS, June 25-27, 2001

The New York Times, *African Nations Widen Medical Help to Women With H.I.V.*, September 1, 2001

John Donnelly, Boston Globe, *In Africa, Free HIV Drug Slow to Reach Babies At Risk Shortcomings Cited in Health Network In Africa, HIV Drug Is Slow To Reach Babies*, September 7, 2001

HIVNET 012 Study Evaluates Viramune (Nevirapine) for Reduction of Mother-to-Child HIV Transmission in Africa

Boehringer-Ingelheim Pharmaceuticals (correspondance)

WOMEN'S TREATMENT ISSUES

Through the AIDS pandemic, a major focus of basic and clinical research has been on the role of small proteins called cytokines in the body's response to infection by HIV. Indeed, some cytokines, most notably interleukin-2, are under investigation as therapeutic agents in the treatment of HIV disease. More recently, a discussion of cytokines has been taking place in regard to women living with HIV. Women with HIV have noted many complaints about abnormal menses (periods). In the past few years, studies have examined menstrual abnormalities in HIV infected women. A recent article in the August 17 issue of *AIDS* presents a broad picture of the biological actions of cytokines in relation to menses.

The article reports the results of a study of 55 HIV-positive women. The study noted a general increase in the number of vaginal cytokines near the time of menses. The researchers measured cytokine levels in plasma and vaginal samples and cytokines appeared to be elevated during menses in comparison with the follicular and luteal phase of the menstrual cycle. This cytokine fluctuation seemed to correlate with vaginal viral load and could account for an increased risk of female-to-male HIV transmission at this phase of the menstrual cycle. The comparison of viral load levels in vaginal secretions to

levels in the blood, to determine whether the vaginal area remains an HIV reservoir, is still being debated because more studies are needed to confirm these facts.

Interleukins (IL)-1-beta, IL-4, IL-6, IL-8 and IL-10, transforming growth factor-beta (TGF-beta), macrophage-inflammatory protein 1 (MIP-1)-beta, RANTES and TNFR-II are the cytokines that appeared to be elevated. The cytokine increases seemed to coincide with an increase in HIV in the female genital tract but not at other sites (plasma and saliva). The researchers advised these patients of the potential additional risk of HIV transmission to their partners during menses and immediately prior to menses and advised them to either abstain from intercourse during those times or take extra precautions in light of the findings.

In response to the limited availability of clinical data on women, the fastest growing population infected with HIV, it is clear that more research needs to focus on how HIV in the female reproductive tract varies with stage of disease and how women at varying stages of HIV are affected by disease changes. This study shows interest in the impact of female physiology on the pathogenesis of HIV, which tends to be understudied. Therefore, it is possible that research on genital viral load in women may continue to be a priority.

Sources: AIDS 2001;15:1535-1543.

Tuomala R et al. Abs 111.7, Cu-Uvin S et al. Abs 111.1, Kovacs A et al. Abs 111.5; Anderson, Palmore M et al. Abs 111.3. Program and abstracts from the 1999 National Conference on Women and HIV/AIDS; October 9-12, 1999; Los Angeles, Calif.

Schuman P, Capps L, Peng G, et al. "Weekly fluconazole in the prevention of mucosal candidiasis in women with HIV infection: A randomized, double-blind, placebo-controlled trial." *Ann Intern Med.* 1997;126:689.

LIPODYSTROPHY

HIV-Positive Individuals and Fat Redistribution: Diet Modification May Be the Key

Body fat distribution refers to the relative proportion of fat tissue in specific regions of the body. Fat distribution has been classified in a variety of ways (examples include: upper body fat versus lower body fat, central fat versus peripheral fat, visceral fat versus subcutaneous fat). The importance of understanding body fat distribution is derived from observations that fat tissue in the different parts of the body affects metabolism differently.

Lipodystrophy, defined as any disturbance of fat metabolism, is associated in some variation with many medical conditions, including HIV/AIDS. While the term "lipodystrophy" is not accurate in its current usage in regard to HIV drug complications, it is widely used since no better word or definition of the condition has yet come along to replace it. Another common phrase for lipodystrophy is "Metabolic Complications of HIV". The condition is sometimes referred to as lipoatrophy (loss of fat), fat redistribution or fat maldistribution syndrome, among others.

A recent study in 85 HIV-infected patients with fat redistribution may link dietary factors and explain their role in the lipodystrophy syndrome. Physical changes associated with lipodystrophy syndrome are related to body shape and body composition, mostly body fat losses and fat gains. No consensus yet exists on the best way to measure these body changes or if body changes are a product of a single process. The ultimate consequences of upper body and visceral fat accumulation are adverse effects on health outcomes, especially those that relate to insulin resistance and cardiovascular disease. Many factors, including sex, race, age, and total body fat content, that affect body fat throughout the body under normal circumstances are thought to be associated with increased fat that is widely and evenly distributed throughout the body..

Of the 85 HIV-infected individuals studied, altered body fat distribution was measured by dietary history, laboratory tests (fasting glucose, insulin, lipids, oral glucose tolerance), standard measurements (mean body mass index, waist-to-hip ratio), and protease inhibitor use, alcohol use, dietary fiber intake, and polyunsaturated-to-saturated fat ratio. The purpose of this study was to compare dietary factors and find an association with insulin resistance. The dietary intake, body composition, and metabolic parameters were measured and the authors found that potential targets for dietary modification include polyunsaturated fats, fiber, and alcohol.

Source:
Hadigan C, Jeste S, Anderson EJ, Tsay R, Cyr H, Grinspoon S.
"Modifiable dietary habits and their relation to metabolic abnormalities in men and women
with human immunodeficiency virus infection and fat redistribution."
CID 2001;33:710

EXPERIMENTAL TREATMENT ISSUES

Low-Dose Oral Shark Cartilage to Treat Kaposi's Sarcoma

As the rates of AIDS-related cancers rise in the United States, more people will look for alternative ways to treat these specific cancers. One alternative method that is currently being studied is the use of shark cartilage. Kaposi's sarcoma (KS) is a tumor that usually appears on the skin and most commonly affects HIV-positive men who have sex with other men. Kaposi's sarcoma is caused by human herpes virus-8, a sexually transmitted virus (HHV-8). Although there is no cure for KS, sometimes the use of highly active antiretroviral therapy (HAART), with or without chemotherapy, can help shrink and control KS lesions.

Physicians at the University Hospitals of Cleveland, Ohio, have recently reported details about treatment of a KS lesion with shark cartilage. According to their case study, a 45-year-old HIV-negative man who developed a KS lesion on his foot was treated with 1 gram of oral ganciclovir, three times daily for three months (because of its possible anti-HHV-8 activity), but this had no effect on his lesion. The patient and his doctors then chose an unconventional approach to KS treatment by using low-dose oral shark cartilage. Researchers monitored the man as he took shark cartilage at a dose of 1,875 mg twice daily for the first three months. The dose was then changed to 1,500 mg three times daily for another 18 months. After three months, the lesion began to shrink and its color faded. By the sixth month it was thinner and almost impossible to notice. No side effects were reported during this time.

Although shark cartilage has been tested in people with cancer, those subjects had received chemotherapy (chemotherapy is known to be successful in combination with shark cartilage), and also had "advanced" cancers of the breast, colon and/or lungs. Research shows that most species of sharks have an extremely low, almost non-existent rate of cancer. Studies have found that the cartilage of the shark may be responsible for this. The proteins in the cartilage can prevent the growth of capillary and other blood vessels. As tumors grow, they must create blood vessels that bring in nutrients and eliminate wastes. If shark cartilage can stop the growth of these vessels, the tumor will starve, eventually killing itself. Special sugars in the cartilage called mucopolysaccharides work with the proteins in the cartilage and are said to stimulate the immune system and help fight disease. KS tumors are often associated with a rich network of blood vessels, so perhaps it is not surprising that several research teams are now studying this therapy because of its potential to reduce blood vessel growth and starve the KS tumor.

Recently, the FDA has approved clinical trials using shark cartilage on non-responsive prostate cancer and Kaposi's sarcoma. Until a controlled clinical trial with HIV-positive individuals takes place, the effectiveness of shark cartilage will be under investigation. Because shark cartilage reportedly blocks the development of new blood vessels, pregnant women and people who have recently suffered a heart attack or have had major surgery recently should not use shark cartilage. Because the above-mentioned patient was HIV-negative, future research needs to examine issues relevant to people with HIV/AIDS, such as drug interactions and the additive effect of chemotherapy. The cost for treatment is approximately \$1.08 and \$1.32 US per day for shark cartilage.

Sources include
Schulz TF. "Kaposi's sarcoma-associated herpes virus (human herpes virus 8):epidemiology and pathogenesis."
Journal of Antimicrobial Chemotherapy 2000;45:15-27

Moses MA, Sudhalter J and Langer R. "Identification of an inhibitor of neovascularization from cartilage." *Science* 1990;248:1408

Browder T, Butterfield CE, Kraling BM, et al. "Antiangiogenic scheduling of chemotherapy improves efficacy against experimental drug-resistant cancer." *Cancer Research* 2000;60(7):1878-1886

Hillman JD, Peng AT, Gilliam AC, et al. "Treatment of Kaposi sarcoma with oral administration of shark cartilage in a human herpesvirus 8-seropositive, human immunodeficiency virus-seronegative homosexual man." *Archives of Dermatology* 2001;137:1149-1152.

INSIGHT AND INFORMATION ON POST EXPOSURE PROPHYLAXIS

Note: In response to the questions received in the past few weeks in regard to Post-Exposure Prophylaxis (PEP), STEP has decided to send out a small briefing on what PEP is and what is the best use for PEP (either occupational use or non-occupational use).

The overall transmission rate of HIV infection following occupational exposure is estimated to be approximately 0.3%. Since the first reported case of seroconversion following occupational exposure to HIV, there have been 315 additional cases of occupationally acquired infection. Several animal studies have shown that the administration of antiviral drugs following, or just before, HIV exposure reduces the rate of viral transmission with varying degrees of efficacy. In addition, a case-control study of healthcare workers in France, the United Kingdom, Italy, and the United States showed that the use of zidovudine (AZT) was associated with an 81% reduction in the risk of HIV infection following occupational exposure. These results have led to the establishment of protocols for the administration of post-exposure prophylaxis (PEP) for HIV infection following occupational exposure.

There is also an increasing body of literature advocating the use of PEP following sexual exposure to HIV, although there are currently no data to support this. PEP is routinely recommended following occupational exposure to HIV. Most PEP regimens involve the use of two nucleoside reverse transcriptase inhibitors with or without the addition of a protease inhibitor. PEP is also increasingly being prescribed following nonoccupational exposure to HIV. It is important that careful risk assessment be performed before prescribing PEP in both the occupational and nonoccupational settings and that risk reduction measures be emphasized. In the last STEP Ezine, we addressed the new guidelines for administering PEP ([see http://www.thebody.com/step/ezone_092101/contents.html](http://www.thebody.com/step/ezone_092101/contents.html)).

Additional Source: *The AIDS Reader* 11(8):402-412, 2001

NATIONAL HIV/AIDS POLICY INFORMATION

AIDS ACTIVISTS AND ADVOCATES MUST HELP OUR ELECTED REPRESENTATIVES REMEMBER AIDS PROGRAMS FOR THE FISCAL YEAR FUNDING (OCTOBER 1, 2001-SEPTEMBER 30, 2002)

AIDS activists are being urged to call their US Representatives and two US Senators during the week of October 1, 2001, to urge them to support the highest possible funding for HIV/AIDS programs. The Congressional subcommittees will start voting on funding levels for HIV/AIDS programs in the very near future. The House Labor-Health and Human Services-Education Appropriations Subcommittee (Labor-HHS), which is responsible for deciding on the level of funding for most HIV/AIDS programs, could meet as early as October 5, 2001, to make decisions for the Fiscal Year 2002. Increases for health programs will be very difficult this year due to severe budgetary constraints. In addition to the difficult job that Congress and the President already have in dealing with the September 11 attack, they will now have to make very hard decisions as to how and by how much to fund critical health programs.

We remain concerned that funding for AIDS programs may be insufficient to address the ongoing and increasing needs of communities affected by HIV and AIDS. Increased funding is critically needed for the Ryan White CARE Act (including the AIDS Drug Assistance Program), the Minority HIV/AIDS Initiative (MHAI), prevention programs at the Centers for Disease Control and Prevention (CDC), and research at the National Institutes of Health (NIH). In order to help, you may call the

Capitol Switchboard at 202-225-3121 or toll-free 800-648-3516 and ask to be connected to your Representative's or Senator's office.

RELIEF FUNDS FOR DISASTER-IMPACTED HEALTH SERVICES

Health and Human Services Secretary Tommy Thompson announced on September 21 that \$126 million dollars will be provided immediately to support services provided in the wake of the September 11 terrorist attack and inflicted disasters. The funds are a part of the total \$5.1 billion dollar disaster-related funds announced by President Bush.

SATELLITE BROADCAST ON HIV PREVENTION

As a part of the Morbidity and Mortality Weekly Report (MMWR) series *Recommendations and Reports*, a satellite broadcast of interest to care and prevention workers will take place on **November 15, 2001, 10:00 AM -12:00 Noon PACIFIC TIME**. This broadcast will include the key recommendations in *Revised Guidelines for HIV Counseling, Testing and Referral*. During this broadcast, implementation issues, resources and recommended reading will also be discussed. Viewers may fax in questions and comments before and during the broadcast. For more information please visit <http://www.cdcnpin.org/broadcast/current/2001/1115/start.htm>.

UPCOMING EVENTS

- October 4, 2001 **IDAHO HIV Conference, Lewiston, Idaho**
CONTACT: Idaho District Health Department 208-799-3100
- October 16, 2001 **AIDS CLINICAL CONFERENCE, Harborview Medical Center**
CONTACT: Kate Willner, kwillner@u.washington.edu
- October 18, 2001 **Tacoma Pierce County Wellness Series**
This is an update for HIV-positive individuals and affected community members to learn more about HIV medications and treatment. This forum will take place at the Willard Resource Center, 3201 South D Street, Tacoma, WA (corner of 32nd and D Street). Call 1-877-597-7837 for more information.
- October 20, 2001 **Youth and AIDS Summit : "Same Name, Different Faces"**
CONTACT: Pierce County AIDS Foundation at 253-383-2565.
- November 4-7, 2001 **CARE/PREVENTION EVENT**
The Forth Annual HIV/AIDS Care and Prevention Event will be held November 4 - 7, 2001 at the Doubletree Hotel on Pacific Highway near SeaTac Airport. For more information call 360-236-3452.
- November 6, 2001 **African American Community Summit on HIV/AIDS**
This is a community-wide event that will address the impact of HIV/AIDS in the African American community. Featured speakers include Dr. Helene Gayle, Dr. Wilbert Jordan, Dr. Maxine Hayes and others. This very important forum will take place at the Miller Community Center, 330 19th Avenue East, Seattle, WA, 98102. Parking, dinner and childcare will be provided. Call 1-877-597-7837 for more information.
- December 2-5, 2001 **North American Treatment Action Forum**

This NMAC sponsored forum will be held in Vancouver, BC at the Sheraton Vancouver Wall Centre Hotel. To register online go to <http://www.nmac.org/nataf/2001/welcome.htm>.

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 Web site 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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