Review

Sex Differences in Adverse Reactions to Antiretroviral Drugs

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Abstract. *There have been recent increases in the number of female participants in HIV clinical trials and the number of studies addressing the influence of sex on HIV infection. The findings of some studies indicate a potential sex difference in the frequency and severity of adverse reactions to antiretroviral drugs. This article reviews the available data on the incidence and characteristics of potential sex differences in adverse reactions to certain nucleoside and nonnucleoside reverse transcriptase inhibitors and protease inhibitors. Adverse effects for which a sex difference has been reported include lactic acidosis, rash, elevation in liver enzymes, dyslipidemia, and insulin resistance. The reasons for these sex differences in adverse drug events are unclear but may include differences between men and women in body mass index and fat composition, hormonal effects on drug metabolism, or the effects of genomic constitutional differences on the levels of various enzymes. These differences warrant further study.*

Introduction

Although the incidence of HIV infection among women is increasing,[1] the proportion of women in clinical trials that evaluate interventions for the treatment of HIV infection and its complications has historically been lower than the proportion of women in the HIV/AIDS patient population. Therefore, most knowledge about the efficacy of antiretroviral drugs and the adverse reactions associated with their use has been derived from studies involving predominantly male subjects.[2,3] A review of female participation in large, multicenter clinical trials found that only 6.7% of the 11,909 AIDS Clinical Trials Group (ACTG) study participants from 1987 through 1990 were women.[4] As a result of the relatively small number of female subjects in earlier HIV clinical trials, little is known about the influence of sex on the natural history of HIV infection and on the incidence and characteristics of adverse drug effects.

Since a 1994 change in the National Institutes of Health policy on the enrollment of human subjects in clinical trials,[5] more women have been involved in HIV-related studies. The proportion of women enrolled in ACTG-funded studies increased from 5.6% in 1987 to 16.9% in 1996.[6] Current estimates are that approximately 20% of participants in ACTG clinical trials are women.[7] However, the proportion of women in these trials still lags behind the proportion (25%) of reported AIDS cases in the United States that occur among women.[8] In addition, several multicenter studies have enrolled exclusively women with or at risk of HIV infection. Examples include the Women's Interagency HIV Study (WIHS), with 2066 HIV-seropositive and 575 HIV-seronegative women[9]; the HIV Epidemiology Research Study (HERS), with 863 HIV-seropositive and 430 HIV-seronegative women[10]; and the Women and Infants Transmission Study (WITS), with 2336 HIV-seropositive women and 1887 infants.[11] Data from several of these studies suggest that sex differences may exist in several aspects of HIV infection and its management, including differences in the tolerability of some antiretroviral drugs.[12-17] This article reviews the incidence and characteristics of sex differences in adverse reactions to antiretroviral drugs used to treat HIV infection.

Nucleoside Reverse Transcriptase Inhibitors

The nucleoside reverse transcriptase inhibitors (nRTIs) were the first antiretroviral drugs introduced into clinical practice and represent the cornerstone of highly active antiretroviral therapy (HAART). These drugs are associated with various adverse effects (Table 1), including myelosuppression, pancreatitis, gastrointestinal (GI) intolerance, peripheral neuropathy, myopathy, and lactic acidosis. Many of these adverse effects are postulated to be mediated through mitochondrial toxicity.[18,19] Some studies have indicated that women are less likely than men to tolerate regimens containing certain nRTIs. In the ACTG 175 trial,[20] monotherapy with zidovudine or didanosine was compared with combination therapy with zidovudine and zalcitabine or with zidovudine and didanosine. Reduction in drug dosage or discontinuation of didanosine-containing regimens because of adverse effects was more common among women than among men. Another study[21] evaluated the incidence of adverse events during nRTI therapy in 1450 subjects with a CD4+ cell count of less than 500/μL. The risk of developing an adverse event related to didanosine was nearly 3 times higher for women than for men (relative risk, 2.7; $P = .03$).

Lactic acidosis is one of the most serious presentations of nRTI-associated mitochondrial toxicity. Although this complication is rare, the associated mortality rate may be as high as 80% when plasma lactate levels exceed 10 mmol/L.[22] The role of sex in the occurrence of this complication has not been directly studied, but a report from the US Food and Drug Admin-

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Table **1.** Clinical Trials on Sex and Nucleoside Reverse Transcriptase Inhibitor-Associated Toxicity

Study	Population	Drugs	Sex Difference in Toxicity
Squires et al: START I and II[12]	78 women, 331 men	Zidovudine or stavudine + lamivudine/indinavir vs stavudine/didanosine/indinavir	Incidence of adverse events higher among women
Currier et al: ACTG 175[20]	438 women, 2029 men	Zidovudine or didanosine or zidovudine/zalcitabine or zidovudine/didanosine	Higher likelihood of reducing dose or discontinuing didanosine-containing regimen among women
Moore et al[21]	392 women, 1058 men	Zidovudine/didanosine/zalcitabine	Nearly 3-fold increase in the risk of an adverse event due to didanosine among women
Boxwell et al[22]	60 patients (50 women, 10 men) with lactic acidosis after treatment with nRTIs	nRTI-containing regimens	83% of cases of lactic acidosis and 85% of the 20 fatal cases occurred in women

ACTG indicates AIDS Clinical Trials Group; nRTI, nucleoside reverse transcriptase inhibitor; START, Selection of Thymidine Analog Regimen Therapy Trials.

istration[23] suggests that women may be at higher risk of lactic acidosis than men. This report found that 83% of 60 lactic acidosis cases in HIV-infected patients treated with an nRTI occurred in women, and 85% of the 20 fatal cases occurred in women. In addition, fatty liver, or hepatic steatosis, occurred in 71% of women, and pancreatitis in 29%.

Nonnucleoside Reverse Transcriptase Inhibitors

The nonnucleoside reverse transcriptase inhibitors (NNRTIs) have become important components of HAART, especially when a protease inhibitor (PI)-sparing regimen is desired. The NNRTI nevirapine is of particular importance to women. This drug is relatively inexpensive and easy to administer and has been shown to significantly reduce the vertical transmission of HIV infection. It is thus an especially attractive option for reducing mother-to-child transmission of HIV, especially in resource-poor countries of the world.[24]

The common adverse effects of NNRTIs are rash and hepatitis (Table 2). Gangar and colleagues[25] were the first to suggest a trend toward a higher frequency of rash among women taking nevirapine than among men taking the drug. Three additional studies provide further support of this sex difference. The first, a multicenter, retrospective cohort study of patients treated with nevirapine,[26] found that 9 of 95 women (9.5%) but only 3 of 263 men (1.14%) experienced a severe rash; the sex difference was statistically significant ($P = .005$). Women had a 7-fold greater risk of severe rash and were 3 to 5 times more likely to discontinue nevirapine therapy than men. A second study[13] assessed the prevalence of skin rash among 280 HIV-infected persons after exposure to nevirapine. The relative risk of rash for women was 11.7 times higher than that for men ($P = .006$). Of the 3 patients who developed Stevens-Johnson syndrome, 2 were women. The third and most recent study[27] reviewed 31 Chinese patients who were taking nevirapine. A nevirapine-associated rash developed in 5 of 8 women (62.5%) but in only 6 of 23 men (26%).

Another concerning adverse effect of NNRTIs is hepatitis, a complication that may be more likely to occur among women taking nevirapine than among men taking the drug. In the FTC-302 study,[28] 468 patients in South Africa were randomly assigned to a regimen of either emtricitabine, an investigational nRTI, or lamivudine, in addition to a background regimen of stavudine and either nevirapine or efavirenz. After 24 weeks of therapy, the incidence of grade 4 elevation in liver enzymes among patients in the nevirapine-containing arm of the study was 9.4%, whereas that among patients in the efavirenz-containing arm was 0%. In the nevirapine-containing arm, the incidence of grade 4 elevation in liver enzymes was 2 times higher for women (12%) than for men (6%; $P = .05$). The 2 patients who died of liver failure were women.

Protease Inhibitors

The introduction of PIs to clinical practice has revolutionized the management of HIV disease. The use of PIs in combination with other antiretroviral agents has led to a substantial reduction in the mortality and morbidity rates associated with HIV infection.[29] The primary toxic effects associated with PIs include GI intolerance, abnormal fat distribution, and metabolic disorders (Table 3).

Several investigators have reported sex differences in the frequency and severity of some of these adverse reactions. In a study[30] of 90 women and 996 men taking ritonavir in combination with reverse transcriptase inhibitors, Currier and colleagues found that men and women experienced similar types of adverse effects. However, the frequency of GI side effects

was higher among women than among men. Nausea, vomiting, and numbness or tingling around the mouth occurred more frequently among women, although diarrhea was more common among men. Another study of ritonavir intolerance in men and women included 93 subjects, 87 of whom were evaluated for adverse events.[31] Ritonavir was associated primarily with GI and neurologic adverse effects. The risk of ritonavir intolerance was significantly higher ($P < .001$) for women (23 of 35; 66%) than for men (14 of 52; 27%).

An analysis of 3 separate trials[32] evaluated the efficacy and tolerability of nelfinavir-containing regimens administered to 78 women and 616 men. The efficacy of nelfinavir in lowering HIV-1 RNA plasma concentrations was similar for men and women. The mean increase in CD4+ cell count was greater among women (116/μL) than among men (84/μL). Although men and women experienced similar types of adverse effects (abdominal pain, diarrhea, pruritus, and skin rash), all of these adverse effects, except for diarrhea, occurred more frequently among women.

Lucas and colleagues also reported a sex difference in the tolerability of PI-containing HAART regimens.[33] This study evaluated the occurrence of treatment failure and adverse drug reactions in HIV-infected persons receiving HAART. No significant difference was found between men and women in plasma HIV-1 suppression: undetectable HIV-1 RNA plasma concentrations were achieved in 37% of the 273 patients. However, the rate of adverse drug reactions was significantly higher ($P = .008$) for women (37%) than for men (25%). The primary adverse effects were GI-related.

Abnormalities in fat distribution and metabolic disorders have been frequently observed in HIV-infected persons treated with HAART. Two prominent clinical features associated with lipodystrophy syndrome are peripheral fat loss and central fat accumulation. Because men and women naturally differ in the amount of body fat and its distribution, it has been speculated that sex differences in these 2 clinical manifestations of lipodystrophy syndrome are likely. A review[14] of 208 HIV-infected patients who experienced lipodystrophy syndrome during HAART found that fat accumulation (in the breast and abdomen) was more common in women and that fat loss (in the limbs and buttocks) was predominant in men. A similar but larger study[34] examined the correlation between sex and morphologic alterations in 2258 HIV-infected persons undergoing antiretroviral therapy. Morphologic alterations (fat loss or fat accumulation) occurred in 33.2% of the subjects but were more common in women than in men, with an adjusted odds ratio of 2.019 ($P = .001$).

Metabolic abnormalities associated with HAART also include hypercholesterolemia, hypertriglyceridemia, insulin resistance, and type 2 diabetes mellitus. In a study[35] designed to examine sex differences in the occurrence of HAART-associated dyslipidemia, 27 men and 13 women who had been taking nelfinavir/didanosine/stavudine for 6 months were tested for lipid abnormalities. A significant increase above baseline ($P < .05$) was found in both sexes for serum concentrations of triglycerides, leptin, and low-density lipoprotein (LDL) cholesterol; these increases were higher among women than among men. Fasting insulin levels and the ratio of LDL to high-density lipoprotein (HDL) cholesterol increased only in female patients ($P < .02$). In contrast, endothelial activation, as measured by circulating E-selectin (cE-selectin) concentrations, showed a larger decrease among men than among women ($P < .02$). As a result, women had higher triglyceride and leptin levels after therapy than did men; in addition, the ratio of LDL to HDL cholesterol and the cE-selectin levels, which had been initially higher among men, were no longer significantly different in men versus women. Although the number of patients in this study was small, the findings suggest that the baseline cardiovascular protection normally enjoyed by women because of a favorable lipid profile may be lost with HAART.

Another adverse event that may be associated with HAART is hypertension, which could be of particular importance for

Table **2.** Clinical Trials on Sex and Nonnucleoside Reverse Transcriptase Inhibitor-Associated Toxicity

Study	Population	Drugs	Sex Difference in Toxicity
Mazhude et al[13]	102 women, 178 men	Nevirapine-containing regimens	11.7-fold increase in risk of skin rash among women; 2 of 3 cases of Stevens-Johnson syndrome occurred in women
Bersoff-Matcha et al[26]	95 women, 263 men	Nevirapine-containing regimens	7-fold increase in risk of rash among women; women were 3-5 times more likely to discontinue nevirapine use
Wong et al[27]	8 women, 23 men	Nevirapine-containing regimens	Higher rate of rash among women
Bartlett J[28]	276 women, 192 men	Emtricitabine or lamivudine + stavudine + efavirenz or nevirapine	2-fold higher incidence of grade 4 elevation in liver enzymes among women than among men on nevirapine-containing regimens

Table **3.** Clinical Trials on Sex and Toxicity Associated with Protease Inhibitors or Highly Active Antiretroviral Therapy

Study	Population	Drugs	Sex Difference in Toxicity
Muurahainen et al[14]	49 women, 159 men	HAART	Women had more fat accumulation; men had more fat loss
Currier et al[30]	90 women, 996 men	Ritonavir + reverse transcriptase inhibitors	Higher rates of nausea, vomiting, and tingling around the mouth but a lower rate of diarrhea among women
Gatti et al[31]	35 women, 52 men	Ritonavir-containing regimens	Greater than 2-fold increase in ritonavir intolerance among women than among men
Gersten et al[32]	78 women, 616 men	Nelfinavir-containing regimens	Women had more abdominal pain and itching; men had more diarrhea
Lucas et al[33]	76 women, 197 men	HAART	Higher rates of adverse drug reactions among women
Galli et al[34]	673 women, 1585 men	HAART	Morphologic alterations more common among women

HAART indicates highly active antiretroviral therapy.

women with HIV infection if further studies confirm that HAART results in a less favorable lipid profile among women than among men. Khalsa and colleagues,[36] in a study of the WIHS cohort, reviewed the incidence and prevalence of hypertension among 2057 HIV-infected women and 569 demographically similar HIV-seronegative women at risk of infection. The baseline prevalence of hypertension was similar among the HIV-seropositive women (14.4%) and the HIV-seronegative women (16.2%; P = not significant). However, multivariate analyses that were controlled for age, ethnicity, and body mass index and that excluded baseline prevalent cases revealed an increase in hypertension after HAART administration for 2 years or more (odds ratio, 1.54; $P < .05$). This increase in hypertension among HAART-treated women was of borderline statistical significance and thus needs to be confirmed in further studies. Nonetheless, the fact that women treated with HAART experience higher rates of dyslipidemia and insulin resistance and may experience a higher rate of hypertension suggests that they may be at greater risk of cardiovascular disease than are men on the same therapy.

Postulated Mechanisms of Sex Differences in Antiretroviral Toxicity

No one knows for certain why sex differences exist in adverse reactions to antiretroviral drugs. Differences in weight and body mass index between men and women may play an important role. Other mechanisms proposed to explain sex differences in the toxicity of drugs in general may also be involved.[37-39] These mechanisms include hormonal changes in women at puberty, during menstrual cycles, and at menopause and the effect of these changes on drug metabolism. Sex differences in fat composition and the impact on drug distribution may also play a role, as may the genomic constitutional difference that exists between men and women and the way in which this difference affects the levels of various enzymes involved in drug metabolism.[40]

Conclusion

The number of women participating in HIV clinical trials and the number of studies designed to address the influence of sex differences on HIV infection are increasing. The results of some of these studies suggest that sex differences may exist in adverse reactions to antiretroviral drugs. More studies are needed to further characterize the specific nature and magnitude of these differences in the toxicity of antiretroviral drugs in women. The mechanisms behind the role of sex in antiretroviral toxicity need to be aggressively evaluated. Finally, the role of therapeutic drug monitoring of antiretroviral drugs needs to be further clarified. Individualized dose regimens based on drug plasma levels may reduce the frequency and severity of some adverse reactions and thus improve the tolerability of antiretroviral drugs for women.

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AIDS Empowerment and Treatment International

An international network of associations of people living with HIV/AIDS

Overview

AIDS Empowerment and Treatment International (AIDSETI) is an international network of 22 associations of people living with HIV/AIDS in 14 African and Caribbean countries. Incorporated in Uganda and in Delaware as a 501(c)(3) not-for-profit organization, AIDSETI aims in the next several years to implement a cross-country program to test the scalability, quality, and cost-effectiveness of an association-based treatment model for HIV. Through this model, all financial, pharmaceutical, and human resources are controlled by local associations. AIDSETI is led by an independent board of 13 directors, the majority of whom are from developing countries. It also maintains a small administrative staff, based in Washington, DC, whose responsibilities include network management and information dissemination. Once the network is fully operational, services provided to HIV/AIDS patients by AIDSETI associations will include the following:

- Psychosocial and nutritional support
- Education on healthy living and survival skills
- Monitoring of disease progression
- Prophylaxis and treatment of opportunistic infections
- Antiretroviral drugs for patients in more advanced stages of disease

AIDSETI will also help conduct operational research to improve referral systems, carry out clinical trials to adapt treatment to resource-poor settings, and ultimately make available a researchable cross-country treatment database. AIDSETI is seeking funding from the Global Fund to Fight AIDS, Tuberculosis and Malaria to cover the majority of costs over the first 3 years of implementation. The network also expects to receive contributions from associations, patients, and other corporate or organizational donors.

Volunteer Opportunities

A printable form on AIDSETI's Web site allows individuals to propose volunteer opportunities or make financial donations. The form is available at www.aidseti.org/ReturnForm1.htm.

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Global AIDS Interfaith Alliance

Web: www.idsociety.org/ATP/Background.htm
Using religious organizations in Africa to help those in rural areas develop HIV prevention and care strategies

Overview

The Global AIDS Interfaith Alliance (GAIA) works through religious organizations in rural Africa to develop village-level action plans for HIV prevention and care. GAIA uses Christian, Muslim, and traditional African religious organizations in its efforts, which are funded through gifts from individuals, foundations, and religious congregations in the developed world. The nongovernmental organization trains rural residents to deliver home-based care, health counseling, pastoral counseling, and support services, as well as to make referrals to testing, diagnostic, and treatment centers if available. In addition, GAIA provides small grants to purchase bicycle ambulances, HIV testing kits, blankets, food, and other supplies.

Volunteer Opportunities

Although GAIA does not formally sponsor the work of health care practitioners from developed countries in the developing world, it can refer volunteers to care facilities in those areas. The group has helped one US-based HIV testing, treatment, and counseling center partner with a rural clinic in Central Africa and would be interested in helping other organizations create similar affiliations.

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Global Strategies for HIV Prevention

Educational efforts to stem HIV transmission in developing countries

Overview

Global Strategies for HIV Prevention is a US-based, 501(c)(3) not-for-profit organization that works to prevent HIV transmission in resource-poor areas of developing countries. The organization's goals include the following:

- Facilitate community programs to prevent mother-to-child HIV transmission
- Sponsor focused workshops and conferences in developing countries on issues relevant to preventing HIV transmission
- Establish programs to prevent HIV infection in women and children who are sexually abused
- Establish prevention programs for health care workers caring for HIV-seropositive patients
- Create mentoring relationships between medical advisors in developed countries and health care workers in developing countries
- Develop and distribute, via all available communication means, HIV information to communities with limited access to educational material

The organization's educational efforts include a CD-ROM entitled "Women, Children and HIV," developed in collaboration with the University of California San Francisco's HIV InSite program. The CD-ROM contains the equivalent of 5000 printed pages of information on categories such as counseling and testing, care of women and children with HIV, prevention, and nutrition. The first edition was distributed to 2000 individuals in 52 countries. The second edition, currently in development, will be distributed to 15,000 individuals and organizations worldwide.

Global Strategies also provides nevirapine to prevent mother-to-child HIV transmission; rapid HIV tests; and antibiotics to treat opportunistic infections. The organization, which is funded through individuals, corporations, foundations, and other grants, has supported programs in more than 20 countries.

Volunteer Opportunities

Global Strategies does not use volunteer physicians to serve patients in the developing world directly. However, volunteers may contribute education, training, and resource information for the educational CD-ROM described above. The organization also welcomes volunteer editors to help confirm the accuracy of such information.

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International Center for Equal Healthcare Access

Volunteer physicians provide health practitioner training in community-based care settings in order to enhance clinical care provided to HIV-infected patients

Overview

The International Center for Equal Healthcare Access (ICEHA) is a US-based, 501(c)(3) not-for-profit organization that represents a network of clinicians from various US medical facilities who donate their time toward improving the quality and expanding the capacity of community-based HIV/AIDS care in developing countries. The organization targets countries where access to antiretroviral drugs is growing. Services provided by ICEHA include medical education and hands-on training for community-based care providers; HIV health literacy and empowerment programs to raise awareness at the village level; and home-based care.

As of November 2002, ICEHA oversaw projects in the following areas:

- *Northern Vietnam:* A medical education and practical training program targets all health care practitioners in Langson province (northern highlands and Chinese border area) in an effort to slow the spread of HIV in the region; if successful, the program may expand nationwide.
- *Côte d'Ivoire:* Medical education is offered to community-based practitioners in the city of Abidjan, who serve roughly 4500 HIV-seropositive patients in a general population of 35,000. An HIV health literacy and health care empowerment program targets 20,000 people in 10 villages in the Bas-Sassandra region.
- *Nigeria:* A program at the rural Ogun-State antenatal clinic to prevent vertical HIV transmission draws on existing antiretroviral services and will serve approximately 3000 pregnant women over a 2-year period.

As of November 2002, ICEHA was considering an additional 5 program proposals. Most projects are scheduled to run 12 to 15

months, although duration varies according to need. ICEHA projects are funded through various sources, including foundations and corporate support.

Volunteer Opportunities

ICEHA is a network of clinicians who donate their time. Current participants practice in the fields of infectious diseases, internal medicine, pediatrics, and obstetrics, among others. Experience levels range from chief residents and fellows to senior-level clinical experts. Medical volunteers work in local clinics, where they provide care while working to train local practitioners by example. A minimum time commitment of 8 weeks is required. Expenses incurred when participating in ICEHA programs may be covered, although reimbursement varies between projects.

Physicians unable to contribute their time may assist ICEHA through financial contributions, distribution of printed materials, and fundraising.

Contact Information

International Center for Equal Healthcare Access
Attention: Marie Charles, MD, MIA, President
PO Box 1139, Princeton, NJ 08542
Phone: 212-243-7234
E-mail: info@iceha.org
Web: www.iceha.org

Médecins Sans Frontières/Doctors Without Borders

Offering HIV prevention, counseling, testing, and antiretroviral treatment through projects worldwide

Overview

Médecins Sans Frontières (MSF) is an international medical aid network that, among its many projects, serves HIV/AIDS patients in developing countries. The organization offers HIV prevention services, especially related to mother-to-child transmission; voluntary counseling and testing; psychosocial support; and prophylaxis and treatment of opportunistic infections. Since 2001, MSF has also provided antiretroviral drugs to HIV-infected patients in Cambodia, Cameroon, Guatemala, Honduras, Kenya, Malawi, South Africa, Thailand, Uganda, and Ukraine. As of December 2002, these programs served almost 2300 patients; in 2003, MSF expects to double the number of countries and patients to which it provides antiretroviral therapy. MSF is a private, not-for-profit organization that receives funding from the public, foundations, corporations, not-for-profit organizations, governments, and international agencies.

Volunteer Opportunities

Approximately 2500 volunteers a year, including physicians, nurses, and other medical personnel, participate in MSF projects around the world. The minimum commitment for a first-time volunteer is 6 months, and commitments of 9 to 12 months are more typical. Volunteer applicants must undergo an in-person interview at an MSF office. Foreign language skills and prior experience in developing or underserved regions are valued.

Volunteer responsibilities vary according to project but generally include a combination of treatment and education.

Contact Information

Médecins Sans Frontières/Doctors Without Borders
Attention: Human Resources Department
6 East 39th Street, 8th Floor, New York, NY 10016
Phone: 212-679-6800
E-mail: field_volunteers@newyork.msf.org
Web: www.doctorswithoutborders.org

MTCT-Plus Initiative

Adding care and treatment to existing programs to prevent mother-to-child transmission of HIV

Overview

Coordinated by Columbia University's Mailman School of Public Health, the MTCT-Plus Initiative aims to add HIV care and treatment to existing programs to prevent mother-to-child transmission of HIV in developing countries. The project, which launched in December 2001, has identified 12 prevention programs in 8 countries (7 in Africa and 1 in Thailand). Beginning in early 2003, pregnant women enrolled in these programs will be offered a post-delivery package of care and treatment services, including education, counseling, prophylaxis and treatment of HIV complications, and antiretroviral therapy where appropriate. Services are offered to women on a lifetime basis, and are also offered to their HIV-seropositive partners and children. The MTCT-Plus Initiative is supported by a coalition of 9 US-based foundations.

Volunteer Opportunities

MTCT-Plus does not currently use physician volunteers from developed countries, although it may do so in the future.

Contact Information

MTCT-Plus Initiative
Attention: Thomas Hardy
Mailman School of Public Health, Columbia University
722 West 168th Street, 4th Floor, New York, NY 10032
Phone: 212-342-0505
E-mail: mtctplus@columbia.edu
Web: www.mtctplus.org

Pangaea Global AIDS Foundation

Working to broaden access to antiretroviral therapy and to support development of an effective HIV vaccine

Overview

The Pangaea Global AIDS Foundation is a US-based affiliate of the San Francisco AIDS Foundation. Launched in May 2000, the nongovernmental organization works in developing countries to broaden access to antiretroviral therapy and other HIV care and to support the development of an effective HIV vaccine. Funding for its efforts comes from private foundations, corporations, individual donors, and the governments of developed countries. Pangaea has projects in Rwanda, South Africa, Uganda, and the Bahamas, where it works in partnership with local medical, academic, and civic organizations to create programs that are sustainable for the long term; culturally relevant and sensitive; locally controlled; and supported by strong management systems, among other considerations. Pangaea's efforts in these 4 countries are described below.

- *Rwanda:* Pangaea's Family HIV Care and Support Project, a joint initiative with the country's Ministry of Health and Office of the First Lady, works with clinics and a hospital in Kigali to provide antiretroviral drugs to HIV-seropositive women and their partners and children.
- *South Africa:* The organization has partnered with hospitals, university medical institutions, and community clinics in the provinces of Kwa-Zulu Natal, Gauteng, and the Western Cape to develop, test, and implement different models of care that include access to antiretroviral drugs.
- *Uganda:* Pangaea has collaborated with Pfizer Inc. and the Academic Alliance for AIDS Care and Prevention in Africa (see above) to create an HIV clinical care and training institute in Kampala. Pangaea is the fiscal agent on an $11 million grant provided by Pfizer for clinic construction.
- *Bahamas:* In partnership with the William Jefferson Clinton Foundation, Pangaea has performed an assessment of the Bahamas' capacity to provide HIV care and developed a plan to provide treatment, including antiretroviral drugs, to local patients beginning in 2003.

Volunteer Opportunities

Pangaea does not currently use physician volunteers from developed countries, although it may do so in the future. Individual physicians can contribute to the organization's efforts by advocating for funding, providing contacts, and assisting in resource solicitation.

Contact Information

Pangaea Global AIDS Foundation
Attention: Vance Yoshida, Director of Development and External Relations
995 Market Street, Suite 200, San Francisco, CA 94103
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E-mail: contact@pgaf.org
Web: www.pgaf.org

Guidelines for Authors and Contributors

The International AIDS Society–USA publishes *Topics in HIV Medicine* as a resource for physicians and other health care practitioners who are actively involved in HIV and AIDS care. The journal is indexed in *Index Medicus*/MEDLINE and is distributed to approximately 12,000 national and international subscribers.

The following guidelines describe the types of articles and contributions published in the journal, outline its policies, and provide instructions for authors. For further information, contact *Topics in HIV Medicine* at topics@iasusa.org.

Categories of Articles

Perspectives. Perspectives articles are summaries of selected talks given at International AIDS Society–USA continuing medical education courses. An International AIDS Society–USA medical writer prepares a summary manuscript from a transcript of the talk. The manuscript is reviewed and edited by the specific course presenter and the journal's appointed peer reviewers.

Reviews. *Topics in HIV Medicine* welcomes unsolicited original review articles on current issues in HIV and AIDS for consideration. *Topics in HIV Medicine* does not publish original research. Manuscripts should be 3000 to 6000 words (excluding references, tables, and figures) and should include numbered references and a brief introductory abstract of approximately 100 to 200 words. Original, adapted, or reprinted figures and tables may be included and should be cited in the text and accompanied by a brief title. Adapted and reprinted work requires the submission of permission obtained from the original publishers and authors. Authors interested in submitting unsolicited manuscripts are encouraged to submit an outline or abstract of the proposed manuscript prior to submission of the completed work; please contact the editor for additional information.

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Stories. Stories for the "Telling Stories" column share the experiences of those involved in HIV and AIDS care. Stories may be approximately 800 to 3500 words and unsolicited submissions are welcome.

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International AIDS Society–USA
425 California Street, Suite 1450
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E-mail: topics@iasusa.org

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Financial Disclosure

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[1]International Committee of Medical Journal Editors. Uniform requirements for manuscripts submitted to biomedical journals. Updated October 2001. Available at http://www.icmje.org. Accessed January 24, 2003.

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Established in 1992, the International AIDS Society–USA is a not-for-profit physician education organization. The mission of the International AIDS Society–USA is to improve the treatment, care, and quality of life of persons with HIV and AIDS through balanced, relevant, innovative, and state-of-the-art education and information for physicians who are actively involved in HIV and AIDS care. The organization's educational activities are particularly intended to bridge clinical research and patient care.

Coming Online and in the May/June *Topics in HIV Medicine:* CROI Summaries

The next issue of *Topics in HIV Medicine* will feature summaries of new research presented at the 10th Conference on Retroviruses and Opportunistic Infections, held February 10 to 14 in Boston, Mass. These articles will also be available online at www.iasusa.org prior to print publication. Topics covered will include:

Basic Science
Mario Stevenson, PhD

HIV Pathogenesis and Vaccine Development
R. Paul Johnson, MD, and Amitinder Kaur, MD

Complications of HIV Disease and Therapy
Judith S. Currier, MD, and Diane V. Havlir, MD

Management of Antiretroviral Therapy
Timothy J. Wilkin, MD, MPH, Mary A. Albrecht, MD, Eoin P.G. Coakley, MD, and Scott M. Hammer, MD

Welcome Remarks by Zinhale Thabethe of South Africa's Sinikithemba Choir

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Thursday, March 20, 2003
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Chairs: Michael S. Saag, MD, and Jeffrey L. Lennox, MD

New York, New York
Friday, March 28, 2003
Hilton New York
Chairs: Gerald H. Friedland, MD, and Paul A. Volberding, MD

Chicago, Illinois
Thursday, April 24, 2003
Hyatt Regency McCormick Place
Chairs: John P. Phair, MD, and Harold A. Kessler, MD

San Francisco, California
Tuesday, May 6, 2003
Hotel Nikko San Francisco
Chairs: Paul A. Volberding, MD, and Stephen E. Follansbee, MD

Washington, DC
Tuesday, May 20, 2003
Marriott at Metro Center
Chairs: Henry Masur, MD, and Michael S. Saag, MD

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