

The National Institute of Allergy and Infectious Diseases

2005-2006 Biennial Report on Women's Health Research

I. Executive Summary

The National Institute of Allergy and Infectious Diseases (NIAID) funds basic and applied research to prevent, diagnose, and treat infectious and immune-mediated illnesses that affect the health of women and girls. NIAID involves women in many of its clinical studies on treatment and prevention of autoimmune diseases, human immunodeficiency virus (HIV) and acquired immunodeficiency syndrome (AIDS), and sexually transmitted infections (STIs). NIAID also collaborates with other organizations on research initiatives aimed at improving women's health.

This summary provides an overview of NIAID's recent accomplishments and initiatives in women's health research. Some of these accomplishments include the expansion of the Autoimmunity Centers of Excellence, the Immune Tolerance Network, and the Autoimmune Disease Prevention Centers; the Phase II/III PRO 2000/5 Gel and Buffer Gel microbicide trials; the sequencing of the *Trichomonas vaginalis* genome and the Phase III clinical efficacy trial of an investigational vaccine for genital herpes, known as the Herpevac Trial for Women. Other initiatives and programs covered in this summary include the Women's HIV Interagency HIV Study, the Center for AIDS Research's Women's Health Supplement, the Microbicides Trials Network, and the HIV Prevention Trial Network in the United States and overseas.

The overview of selected NIAID-sponsored women's health activities, as well as scientific advances is presented here in two separate focus areas: scientific accomplishments, which include HIV/AIDS, STIs, and immunology and immune-mediated diseases and related accomplishments in women's health research, which include research training, and the women's health research work group. There is also a section on initiatives which includes program announcements, requests for application, contracts and conferences.

II. Scientific Accomplishments

A. Human Immunodeficiency Virus/Acquired Immunodeficiency Syndrome (HIV/AIDS)

Worldwide, women face the greatest risk of acquiring HIV due to substantial mucosal exposure to seminal fluids, prevalence of non-consensual sex, and sex without condom use. Compounding these risks for women are the unknown risk behaviors of their male sexual partners. The number of women with HIV infection and AIDS has been increasing steadily worldwide.

In addition to the complications of AIDS that afflict men, infected women also suffer gender-specific manifestations of HIV disease such as recurrent vaginal yeast infections, pelvic inflammatory disease, genital ulcer disease, severe herpes infections, gender-specific abnormalities related to infection with human papillomavirus, as well as vulvar and vaginal carcinomas. Drug metabolism has also been shown to differ in women as compared to men, potentially resulting in differential responses to antiretroviral therapy and an increased incidence of drug toxicities in women. Frequently, women with HIV infections have difficulty accessing health care and carry a large burden of caring for children and other family members who may also be HIV-infected. They often lack social support and face other challenges that may interfere with their ability to adhere to treatment regimens.

NIAID is supporting investigations of the course of HIV/AIDS in women through multiple initiatives including intramural studies, unsolicited research on Women and HIV/AIDS as well as the Women's Interagency HIV Study (WIHS), a long-term cohort study, the Centers for AIDS Research (CFAR) women's health supplement and clinical trials to investigate gender-specific differences in HIV disease progression, complications and/or treatment. These clinical trials are being conducted by the Microbicides Trials Network, the Adult AIDS Clinical Trials Group, the Pediatric AIDS Clinical Trials Group, and the Community Programs for Clinical Research on AIDS.

1. Epidemiological Research

NIAID-supports epidemiological research on:

- The long-term natural and treated history of HIV infection in women, in particular research that evaluates the impact of antiretroviral therapy (ART) on the clinical course of HIV disease.
- The effect of hormonal, endocrine, and local factors on viral load and sexual transmission.
- Studies on older populations of HIV-infected women to investigate what pathogenic processes are related HIV, ART, and/or the aging process.
- Characterization of acute clinical events and concomitant infections and their impact on HIV disease progression.
- Studies of the female genital tract compartment including the microenvironment, HIV virology and immunology of the female genital tract as compared to blood.

Women's HIV Interagency Study

The NIAID supports researchers who study the unique features of HIV/AIDS in women through the Women's Interagency HIV Study (WIHS). WIHS is the largest observational study of HIV-infected women in the United States. The majority of the women who participate in the study are African American and Latina women living in urban areas. This study has yielded many major results that have led to a better understanding of how HIV is spread, how the disease progresses and how it can best be treated. The Women and Infant Transmission Study (WITS), a large cohort study that was funded by NIAID, is being phased-out. The National Institute of Child Health and Human Development (NICHD) will support a long-term follow-up to the Study.

Scientific Advances

Association of Cigarette Smoking with HIV Prognosis among Women in the Highly Active Antiretroviral Therapy (HAART) Era

Researchers analyzed data from the WIHS study to assess the association of cigarette smoking with the effectiveness of HAART among low income minority women. Those women who participated in the study were followed for over 7 years and represented 72 percent of all women who initiated HAART between 1995 and 2003. After controlling for age, race, hepatitis C infection, illicit drug use, previous antiretroviral therapy, and previous AIDS, researchers found that smokers on HAART had poorer viral responses and poorer immunologic responses than non-smokers. There was a greater risk of virologic rebound and more frequent immunologic failure observed among smokers. These findings indicate that some of the benefits of HAART are negated in HIV- infected women who smoke cigarettes. (Am J Public Health. 2006 Jun; 96(6):1060-1065)

2. Prevention Research

a.) Topical Microbicides

Current global estimates of people infected with HIV are exceeding 38 million, with the majority of these infections in women. In Africa, the proportion of women infected with HIV has exceeded 50 percent, and the most at risk women appear to be those in marriages with partners who engage in sex outside of marriage. Thus, there is an intensified need for the development of a safe, effective and acceptable topically applied chemical and/or biologic barrier to prevent sexually transmitted HIV infection. A topical microbicide is a preparation (e.g., gel, cream, film, or foam) that is applied to the vagina or rectum to inactivate or inhibit STI pathogens, including HIV, that are being transmitted by either sexual partner. It is believed that topical microbicides might be more effective than condoms in preventing HIV infection because they would be easier to use and women would not have to negotiate their use, as they must often do with condoms. Microbicides may also provide protection to men who have sex with men and women. The ideal microbicide would be safe and non-irritating to the mucosal tissues, even if used on multiple occasions in a short period of time. In addition, they would be inexpensive, unobtrusive in use, both fast- and long-acting, easy to store, and appealing to potential users. Topical microbicides should be available in both spermicidal and non-spermicidal formulations so that women would not have to put themselves at risk for acquiring HIV and other STIs in order to conceive a child.

NIAID-sponsored research goals support the development of a topical microbicide that:

- prevents infection and/or viral replication by both cell-free infectious HIV particles and cell-associated infectious particles;
- is safe and non-inflammatory (causes no irritation to the vaginal/cervical/urethral/rectal epithelium); and
- reduces transmission and acquisition, including potentiation of HIV acquisition by other STIs.

Scientific Advances

Protection of Monkeys from Vaginal SHIV Challenge by Combinations of Vaginally Delivered Inhibitors of Virus-Cell Fusion.

Taking three microbicides that target HIV cell entry targets, researchers showed that although each of the three molecules individually displayed some level of protection from infection, combinations of 2 or all 3 microbicide candidates were more effective at preventing vaginal transmission of SHIV in monkeys. This work has provided the first *in vivo* proof that combination microbicides can be more effective than individual microbicides. (Nature, **438**:99-102, 2005.)

Bioengineering Lactobacilli to Secrete the HIV Inhibitory Protein Cyanovirin-N

Cyanovirin-N (CVN) is a protein purified from extracts of the cyanobacterium (blue-green alga) *Nostoc ellipsosporum*. *In vitro* and *in vivo* studies have shown CVN to be a highly potent inhibitor of HIV replication and transmission. One method that addresses barriers to deployment of a protein-based microbicide is bioengineering of naturally occurring *Lactobacilli* to act as a carrier, production and delivery system. The CVN secreted by bioengineered *Lactobacilli* were found to maintain CVN's inhibitory properties. These studies have significantly expanded the scope of bioengineered *Lactobacilli* as a producer and delivery system for microbicides. (J. Acquir. Immun. Defic. Syndr. **40**: 512-520, 2005)

Use of Frozen Cervical Tissues for Microbicide Testing in Cervical Explant Assays

The cervical explant (where a tissue is moved from its original site and transferred to an artificial medium for growth) tissue-based *ex vivo* organ culture method has become an important assay for assessing the potential efficacy and toxicity of candidate microbicides. The work by NIAID-sponsored researchers has shown that cervical tissues can be frozen and then used after thawing for assessing microbicide efficacy and safety. The ability to use frozen cervical tissues without significant loss of tissue integrity or susceptibility to HIV infection greatly increases the utility and potential availability of these tissues for microbicide studies by allowing collection and storage of tissues for future use. (AIDS Res. Hum. Retroviruses **22**:419-424, 2006.)

Clinical Trials

Microbicide Trials Network

As part of the newly restructured HIV/AIDS clinical trials networks, an award was made to Magee-Womens Research Institute, to lead the Microbicide Trials Network (MTN). Using a drug development model, the MTN will develop a highly focused microbicide research and development strategy to advance the most promising microbicides toward licensure for prevention of HIV acquisition and transmission.

Phase II/IIb Safety and Effectiveness Study of the Vaginal Microbicides BufferGel and 0.5% PRO2000/5 Gel (P) for the Prevention of HIV Infection in Women

A clinical trial entitled "Phase II/IIb Safety and Effectiveness Study of the Vaginal Microbicides BufferGel and 0.5% PRO2000/5 Gel (P) for the Prevention of HIV Infection in Women" is ongoing. The primary objectives of this trial are: (1) To evaluate the safety of BufferGel and 0.5% PRO2000/5 Gel (P) when applied intravaginally by women at risk for sexually-transmitted HIV infection; and (2) To estimate the effectiveness of BufferGel and 0.5% PRO 2000/5 Gel (P) in preventing HIV infection among at-risk women. Approximately 3,220 women total will take

part in the study, 800 of whom will take part in the Phase II portion of the study. Enrollment in the Phase II portion of the study, conducted as an uninterrupted lead-in to the Phase IIb portion, has been completed. Enrollment in the Phase IIb portion is ongoing at sites in Philadelphia, PA; Lilongwe and Blantyre, Malawi; Harare and Chitungwiza, Zimbabwe; Lusaka, Zambia; and Durban and Hlabisa, South Africa. More information is available at: www.hptn.org/research_studies/hptn035.asp

Phase II Expanded Safety and Acceptability Study of the Vaginal Microbicide 1% Tenofovir Gel

A clinical trial entitled "Phase II Expanded Safety and Acceptability Study of the Vaginal Microbicide 1% Tenofovir Gel" was initiated in New York City, New York; Birmingham, Alabama; and Pune, India. The primary objective of the study is to assess the safety of tenofovir gel for vaginal use in HIV-uninfected women versus a placebo gel when used once daily or prior to intercourse. The full protocol is available at: www.hptn.org/research_studies/hptn059.asp.

The Sexually Transmitted Infections Clinical Trials Group (STI CTG)

The Sexually Transmitted Infections Clinical Trial Group is preparing to initiate a Phase I trial to evaluate the safety of a twice daily, vaginally applied, microbicide gel. The proposed indication of this topical microbicide is the prevention of genital herpes. This microbicide is being tested in conjunction with the Division of AIDS (DAIDS) and with a proposed indication for prevention of HIV transmission.

HIV Microbicide Design and Development Teams

The single award of the milestone-driven program entitled "HIV Microbicide Design and Development Teams" was awarded to Starpharma LTD. In the first year of funding a clinical trial entitled "A Phase 1, Placebo Controlled Study of the Safety of 3% w/w SPL7013 Gel, and administered to the Penis of Healthy Male Volunteers Once Daily for Seven Days" was initiated at the Melbourne Sexual Health Clinic in Australia. In addition, other preclinical milestones for manufacturing and toxicity studies have been met.

HIV Prevention Preparedness Study

Accrual in the HIV Prevention Preparedness Study has been completed at 4 international sites in Zambia, South Africa and Tanzania. The purpose of this study is to assess the ability of sites to recruit and retain participants for future efficacy trials of topical microbicides and to develop reliable data on HIV seroprevalence and seroincidence in the target populations. Data analysis and manuscript preparation are underway. The full protocol is available at: www.hptn.org/research_studies/hptn055.asp.

b.) Prevention of Mother-to-Child Transmission (MTCT) of HIV

Almost all HIV-infected children acquire the virus from their mothers before or during birth or through breastfeeding. In the United States, approximately 25 percent of pregnant HIV-infected women not receiving antiretroviral therapy passed on the virus to their babies. The rate is significantly higher in developing countries. Most MTCT, estimated to cause more than 90 percent of infections worldwide in infants and children, occurs late in pregnancy or during birth. Although the precise mechanisms are unknown, scientists think HIV may be transmitted when maternal blood enters the fetal circulation or by mucosal exposure to virus during labor and delivery. The role of the placenta in maternal-fetal transmission is unclear and the focus of ongoing research.

The risk of MTCT is significantly increased if the mother has advanced HIV disease, increased levels of HIV in her bloodstream, or fewer numbers of the immune system cells-CD4+ T cells-that are the main targets of HIV.

In general, in developing countries where safe alternatives to breastfeeding are not readily available, the benefits of breastfeeding in terms of decreased illness and death due to other infectious diseases greatly outweigh the potential risk of HIV transmission. In HIV-infected pregnant women, the safety and pharmacology of these potent drug combinations need to be better understood, and NIAID is conducting studies in this area.

NIAID-sponsored research goals on the Prevention of Mother-to Child HIV Transmission focus on:

- Defining the mechanisms and risk factors for HIV transmission to children and adolescents, and from mother to infant, as well as risks for disease progression within the framework of clinical studies and trials.
- Developing and testing additional ARV strategies to prevent mother to infant HIV infection through clinical trials in the United States and international settings.
- Developing interventions for prevention of HIV transmission via breast milk in settings where breastfeeding is the best assurance for infant nutrition.

Scientific Advances

Combining Preventing Maternal To Child Transmission with Active Case Finding for Tuberculosis

Tuberculosis (TB) is the preeminent manifestation of HIV infection and has become a leading cause of maternal mortality and morbidity in high HIV-prevalence settings. Active TB in pregnant women has potentially serious consequences for fetuses and newborns. In Soweto, South Africa, there is a more than 90 percent uptake of voluntary counseling and HIV testing during routine antenatal care, and almost one third of pregnant women are HIV-infected. The posttest counseling session of the prevention of mother-to-child transmission program provides an opportunity to screen HIV-infected pregnant women for TB. In this study, 370 HIV-infected pregnant women were screened for symptoms of active TB by lay counselors at the posttest counseling session. If symptomatic, they were referred to nurses who investigated them further. Eight women were found to have previously undiagnosed, smear-negative, culture-confirmed TB. Researchers found that rates of TB in HIV-infected pregnant women are high, and screening for TB during routine antenatal care should be implemented in high HIV-prevalence settings. Active, undiagnosed TB is a clinically significant public health problem in HIV-infected pregnant women in Soweto. This study shows that symptomatic TB screening is feasible and should be considered for incorporation into routine antenatal VCT and clinical care of HIV/TB co-infected women and children. (*J Acquir Immune Defic Syndr* 42(3):379-381 (2006))

3. The Center for AIDS Research (CFAR)

The Centers for AIDS Research program is a unique infrastructure program to support a multidisciplinary peer-reviewed AIDS research environment that coordinates studies, promotes communication, provides shared services/expertise, and funds short term feasibility studies that cannot be funded easily by other funding mechanisms. The CFAR program has supported a women's health research supplement that funded numerous pilot projects on women's health and AIDS research. Several accomplishments are listed as follows:

Tufts University's and Brown University's CFAR's women's health research supplement has helped support the establishment of an HIV and menopause Clinic. The clinic aims to assemble a cohort of HIV-infected menopausal women that will help answer issues of osteoporosis/osteopenia, and cardiovascular complications in the setting of HIV and menopause.

The HIV and Women's Health Working Group at the **University of North Carolina, Chapel Hill, CFAR**, is focused on aspects of HIV infection in women, including the role of family, domestic violence, poverty, menopause, gender roles, and other social conditions that surround women with HIV, as well as a particular focus on the pharmacology of antiretroviral therapy in the genital tract of HIV-infected women. This group is in the process of opening a Women's Comprehensive Care Clinic with a research focus on increasing the recruitment, enrollment, and retention of women into HIV clinical trials.

Through pilot project awards and supplements funded through the Centers for AIDS Research (CFAR) Developmental Core the following MTCT studies are underway: "HIV Risk factors and reduction of MTCT in Tomsk, Siberia," "Efficacy of cognitive-behavioral interventions for HIV infected mothers in South Africa," and "Infant immunization to reduce pneumonia in HIV+ women".

B. Sexually Transmitted Infections

The prevention and treatment of sexually transmitted infections (STIs) are critical global and national health priorities because of their devastating impact on women and infants and their inter-relationships with HIV/AIDS.

STIs and HIV are linked both by biological interactions and because both infections occur in the same populations. Infection with certain STIs can increase the risk of HIV acquisition and transmission as well as alter the course of disease progression. In addition, STIs can cause long term health problems, particularly in women and infants. Some of the sequelae of STIs include pelvic inflammatory disease (PID), infertility, tubal or ectopic pregnancy, cervical cancer, and perinatal or congenital infections in infants born to infected mothers.

NIAID supports research for more effective prevention and treatment approaches to control STIs. This includes:

- research for safe and effective vaccines, topical microbicides, therapeutics, and strategies for preventing and treating STIs and their sequelae;
- basic research on pathogenesis, immunity, molecular and structural biology of sexually transmitted pathogens and the impact of STIs in various populations; and
- development of better and more rapid diagnostics.

Each year, an estimated 15 million Americans suffer the effects of STIs at a cost exceeding \$16 billion. Recent studies indicate that the more prevalent STIs that cause non-ulcerative diseases (chlamydia, gonorrhea, and trichomoniasis), as well as the STIs that cause ulcerative diseases (syphilis and chancroid), increase the risk of HIV transmission by at least two- to five-fold.

Because some infectious agents (e.g., *Chlamydia trachomatis*) can ascend to the upper female genital tract, the long term consequences of infection are also more severe for women and may result in PID, infertility, or tubal/ectopic pregnancy. The harmful effects on babies born to infected mothers may include stillbirth, premature birth, and perinatal and congenital infections. Moreover, many infections are often asymptomatic in women, resulting in a delay or lack of treatment. Women and children bear a disproportionate burden of the harm caused by STIs. Group B streptococci (GBS) also cause infections in mothers during pregnancy as well as in the neonate. During pregnancy, women can be afflicted with amnionitis, endometritis, sepsis, and meningitis. Intrauterine infections from GBS can lead to stillbirth or sepsis. In addition, infants can also be infected with GBS during passage through the birth canal resulting in sepsis, pneumonia and/or meningitis.

NIAID supports a broad array of biomedical research focused on the STIs. Selected significant advances in sex- and gender-specific STI research are provided.

1. Genital Herpes

There are two types of herpes simplex virus (HSV) and both can cause genital herpes. HSV type 1 (HSV-1) most commonly infects the lips, causing sores known as fever blisters or cold sores, but it also can infect the genital area and produce sores. HSV type 2 (HSV-2) is the usual cause of genital herpes, but it can also infect the mouth. HSV-2 is more common in women (approximately one out of four women) than in men (almost one out of five). Genital HSV infections can present serious health consequences including lifelong recurrent episodes of painful, genital lesions, increased likelihood of HIV transmission and acquisition, and for women, possible transmission to fetus or neonate that can result in neonatal brain damage or death.

The 1994-2004 Center for Disease Control and Prevention's (CDC) surveillance results showed the overall seroprevalence of HSV-2 to be 17 percent, which is a substantial decrease from the seroprevalence rate of 21 percent in 1988-1994. Decreases in HSV-2 seroprevalence were prominent among the 14-19 age group and continued through the young adult age group, even after adjusting for changes in sexual behavior. This promising data shows the trajectory of increasing HSV-2 from the 1988-1994 has been reversed. [JAMA, 2006; (296 Vol.8): 964-973].

Clinical Trials

Herpevac Clinical Trial for Women

A pivotal phase III double-blind clinical efficacy trial of an investigational vaccine for the prevention of genital herpes is enrolling 7550 women at approximately 42 sites in the United States and Canada. This study, which is known as the Herpevac Trial for Women (<http://www.niaid.nih.gov/dmid/stds/herpevac>), is being conducted as a public private partnership with GlaxoSmithKline.

2. Human Papillomavirus

Human papillomavirus (HPV) is the name of a group of viruses that includes more than 100 different strains. More than 30 of these viruses are sexually transmitted, and they can infect the genital area of men and women. Most people who become infected with HPV will not have any symptoms and will clear the infection on their own. Some of the viruses are called “high risk” types and can lead to cancer of the cervix, vulva, vagina, anus or penis in addition to Pap test abnormalities. “Low risk” types of HPV may cause mild Pap test abnormalities or genital warts.

HPV is of clinical and public health importance because persistent infection with certain oncogenic types can lead to cervical cancer. Cervical cancer is one of the most common cancers in women worldwide. On June 8, 2006, an HPV vaccine was licensed by the Food and Drug Administration (FDA) for use in females, ages 9-26 years. Gardasil is the first vaccine developed to prevent cervical cancer, precancerous genital lesions and genital warts due to HPV types 6, 11, 16 and 18.

Scientific Advances

Condom Use Reduces Risk of genital HPV infection in young women

NIAID-sponsored researchers evaluated whether the use of the male condom reduced the risk of male-to-female transmission of HPV infection. This study followed young women who reported their sexual activities just prior to and during the study period. Cervical and vulvovaginal samples for HPV DNA and Pap smear testing were collected and sexual behavior was recorded in electronic diaries. Research results suggest the incidence of genital HPV was lower among women whose partners used condoms for all instances of intercourse as compared with those women whose partners used condoms less than five percent of the time. These findings suggest that among newly sexually active women, consistent condom use by their partners appears to reduce the risk of cervical and vulvovaginal HPV infection. (NEJM 354(25):2645-2654, 2006)

3. Chlamydia

Chlamydia trachomatis infections are among the most prevalent of all STIs. In women, chlamydial infections may result in PID, which is a major cause of infertility, ectopic pregnancy and chronic pelvic pain. The rate of reported chlamydial infection is greater among women than men, and adolescent women are at the highest risk of infection. Asymptomatic infection is common in both men and women. In the United States, the continuing increase in reported chlamydia cases is likely to represent expansion of screening for the infection, the development of more sensitive screening tests, and more complete national reporting.

Scientific Advances

Chlamydia protein offers a neutralizing antigen

Chlamydia trachomatis is the leading cause of bacterial sexually transmitted disease and infectious preventable blindness. Despite decades of effort, there is no vaccine against *C. trachomatis* diseases. In this study, researchers conducted an investigation of a protein, polymorphic membrane protein D (PmpD) that was described decades ago as being found across multiple chlamydia strains. The results from this study indicate antibodies specific to this particular protein are neutralizing *in vivo*, but this action is blocked *in vitro*, suggesting that a decoy-like immune evasion strategy may be active *in vivo*. These results suggest a vaccine protocol using this recombinant protein (PmpD) to elicit neutralizing antibodies might offer protection from many or all strains of Chlamydia and possibly surpass the level of protection achieved through natural immunity. This basic research may provide an important step towards the development of a vaccine against Chlamydia infections. (PNAS 2006; 103; 1894-1899)

4. Chancroid

Chancroid is an acute ulcerative disease caused by *Haemophilus ducreyi*. It is endemic in many parts of the developing world and is an important risk factor for heterosexual spread of HIV. Chancroid usually occurs in discrete outbreaks in the United States, although the disease is endemic in some areas.

Scientific Advances

Immunization with the *Haemophilus ducreyi* Hemoglobin Receptor HgbA Protects against Infection in the Swine Model of Chancroid.

The sexually transmitted infection chancroid facilitates the spread of HIV in populations where both chancroid and AIDS are endemic. Thus, successful efforts to prevent chancroid may lower HIV infection rates in these populations. The etiologic agent of chancroid is *Haemophilus ducreyi*. Using a swine model of *H. ducreyi* infection, researchers demonstrated that an experimental HgbA vaccine prevents chancroid, as determined by several parameters including histological examination and measurement of antibody activity. Anti-HgbA immunoglobulin G blocked hemoglobin binding to *H. ducreyi*'s HgbA receptor, suggesting a novel mechanism of protection that works by limiting iron acquisition by the pathogen. This study provides the first example of a vaccine for chancroid with significant efficacy in an animal model. Taken together, these data suggest continuing the development of an HgbA vaccine to prevent chancroid. Such a vaccine strategy might also be applied to other bacterial pathogens with strict iron requirements. (*Infection and Immunity*_74(4): 2224-2232, 2006.)

5. Trichomoniasis

Trichomoniasis is a sexually transmitted infection that affects both men and women and results in approximately 7.4 million new cases, in the United States. The trichomoniasis infection commonly occurs in a woman's vagina, resulting in a vaginal discharge, vaginal odor, discomfort during sexual intercourse and urination, irritation and itching of the genital area and, in rare cases, lower abdominal pain. Both men and women with trichomoniasis have an increased susceptibility to HIV infection and many transmit HIV to their sexual partners. Pregnant women with the infection may deliver a low weight or premature infant. Although prescription drugs cure trichomoniasis, drug resistance has become an increasing concern.

Scientific Advances

Scientists Sequence Genome of Parasite Responsible for Trichomoniasis

NIAID-sponsored researchers have decoded the genetic makeup of the parasite that causes Trichomoniasis, one of the most common STIs, revealing potential clues as to why the parasite has become increasingly drug resistant and suggesting possible pathways for new treatments, diagnostics and a potential vaccine strategy. (JM Carlton et al. Draft genome of the sexually transmitted pathogen *Trichomonas vaginalis*. *Science* DOI:10.1126/Science.1132894(2007)

C. Immunology and Immune-mediated Diseases

The immune system is important at all stages of life in fighting disease-causing microorganisms or pathogens, including: viruses, bacteria, fungi, and parasites. The immune system discriminates self from non-self; however, women are able to carry a fetus without rejection. This ability seems to be at odds with the fact that women also suffer much more commonly than men from autoimmune diseases, where the immune system attacks its own tissues. In addition, many of the autoimmune diseases are more common after the onset of puberty or in middle to late life, times of changes in the hormonal environment in women. Pregnancy may exacerbate or ameliorate several immunologic diseases, including autoimmune diseases and asthma and allergic diseases. In addition, increased understanding of the mechanisms of natural maternal-fetal tolerance may allow the development of new strategies for the induction of clinical tolerance and autoimmune disease. NIAID supports a number of investigations on immunology and immune-mediated diseases and their effect on women's health. Selected accomplishments are provided in this section of the report.

1. Autoimmune Diseases

A. Lupus

Systemic Lupus Erythematosus (SLE), more commonly known as Lupus, is an inflammation of the connective tissues in the body. Lupus can afflict every organ system and is nine times more common in women than in men. Lupus affects black women three times as often as white women.

Scientific Advances

Study of estrogen effects on B cells in Lupus

Results from the SELINA study (Safety of Estrogen in Lupus Erythematosus National Assessment) demonstrate that estrogen can exacerbate lupus. Researchers are investigating those lupus patients who develop multiple disease flares while on estrogen in comparison to those lupus patients whose disease is not hormonally modulated. Researchers are analyzing B cell function after exposure to estrogen and are looking for polymorphisms in genes that are associated with susceptibility to estrogen-induced worsening of disease. Studies of this type may permit researchers to better identify lupus patients at risk for estrogen-induced disease flares as well as identify cellular pathways involved in disease flares. (*New England Journal of Medicine*; Dec. 2005; 353(24):2550-8)

Germinal center exclusion of autoreactive B cells is defective in lupus

Researchers have found a failure of B cells to mount an immune response to a foreign substance is central to the pathogenesis of lupus. This failure on the part of B cells is referred to as B cell tolerance. The subversion of B cell tolerance is poorly understood because of difficulties associated in identifying relevant autoreactive B cells and in obtaining lymphoid tissue. Scientists used tonsil biopsies, to circumvent this limitation, because B cells found in these biopsies were found to be abnormally regulated in lupus patients. This faulty regulation was not shared in rheumatoid arthritis patients. This type of research represents the first comparative analysis of the fate of a specific autoreactive B cell in the human population. This study addresses an important question about the origin of autoantibodies in lupus patients, which are thought to be due to the production of pathological autoantibodies. The researchers demonstrated that autoreactive B cells in lupus patients do not stop at a specific developmental checkpoint but proliferate, mature, and secrete pathogenic autoantibodies. Novel lupus therapies may focus on strengthening this checkpoint as a way to prevent lupus flares. (*J. Clin Invest.* 115:3205-16. Epub Oct 6 (2005).

Regulation of B cell tolerance by the lupus susceptibility gene

In this study, researchers demonstrated that a protein (Ly108), found in immature B cells, is unable to cause cell death triggered by binding antigen, which impairs a mechanism that removes autoreactive B cells. It may be possible to design drugs that increase this protein's activity as a means to provide new drug therapies for lupus patients. (*Science* 312: 1665-9(2006))

B. Autoimmune Disease of the Ovaries

Ovarian autoimmune disease is associated with premature menopause and is linked to unexplained infertility. While some cases of premature menopause have a genetic basis, or are due to chemotherapy, studies suggest that half of all cases of premature menopause are due to an autoimmune attack on the ovaries. In addition, approximately half of all women with unexplained infertility have antibodies that react specifically with the ovaries.

Scientific Advances

Association of unexplained infertility with gonadotropin and ovarian antibodies

Scientists have gathered compelling evidence for an autoimmune disease of the ovary. Ovarian autoimmunity may affect as many as 1-2 million women in the United States. To determine the relationship between ovarian and gonadotropin autoantibodies and unexplained infertility, researchers analyzed the ovary specific antibodies found in the blood of patients with unexplained infertility and a comparison group from a blood bank. Patients with unexplained infertility had either no gonadotropin treatment or two or more gonadotropin cycles to induce ovulation. There was no significant difference in ovarian autoantibodies between women who were treated with gonadotropin and those women who did not receive the treatment. While gonadotropin autoantibodies were significantly more

frequent in women who received the gonadotropin treatment, but also present, to a lesser extent, in untreated infertile patients. The findings suggest that gonadotropin antibodies may represent a separate marker of ovarian autoimmunity in unexplained infertility. These types of research further the study of disease pathogenesis of ovarian autoimmunity and contribute to a better understanding of an autoimmune disease that affects women's health. (*Am J Reprod Immunology*. 2006 Nov-Dec; 56(5-6): 289-91)

Clinical Trials

NIAID is supporting three clinical trials in stem cell transplantation to evaluate autologous hematopoietic stem cell transplantation for the treatment of three autoimmune diseases: scleroderma, systemic lupus erythematosus, and multiple sclerosis. These complex trials, which opened in FY 2006, will also include studies of the underlying immune mechanisms of these diseases and treatments.

2. Asthma and Allergies

The latest statistics show that asthma is on the rise. According to the U.S. Centers for Disease Control, more than 20 million Americans currently have asthma and another 10 million have been diagnosed with asthma at some point in their life. Roughly 6.5 million American children, or nearly 9 percent of the nation's pre-adult population, have asthma. NIAID sponsored researchers are investigating immune responses to asthma and other allergic conditions.

Scientific Advances

IL-1R Antagonist Gene and prenatal smoke exposure are associated with childhood asthma

To gain a greater understanding of the mechanism for allergic asthma and other allergic diseases, researchers conducted genetic association studies using DNA from children with and without allergic diseases. In addition, researchers measured interactions between genes and smoking using the interleukin-1 receptor antagonist (IL-1R) gene polymorphisms to identify risk for pediatric asthma and bronchial hyperresponsiveness. In the analysis, the IL-1R gene was not found to be associated with asthma. However, in the stratum of maternal smoking during pregnancy, the genotype significantly increased the relative risk of asthma in children, both in repeated asthma occurrences and persistent asthma. Researchers found that in the first decade of life, the gene-environment interaction of the IL-1R gene and maternal smoking during pregnancy increased the risk of childhood asthma. (*Eur Respir J*. 2006 Nov 15)

3. Preventing Immune-mediated pregnancy complications

Pregnancy constitutes a major challenge to a mother's immune system because it requires tolerance of antigens encoded by the prospective father's genes. Failure of immune tolerance is a possible cause for recurrent miscarriages, high mortality and morbidity rates at birth, as well as long term development delay and metabolic disorders during adult life.

Scientific Advances

Using an antibody-independent mouse model of spontaneous miscarriage, researchers are exploring how the activation of the inflammatory system leads to defective placental development. These studies provide the first evidence linking complement activation to an angiogenic factor imbalance associated with placental dysfunction, thus opening the way to monitor levels of complement activation in the serum of pregnancy women as a tool to predict and prevent immune-mediated pregnancy complications. (*J. Exp. Med.* 2006 Aug 21; 203(9):2165-2175)

4. Research on Immunity in the Female Reproductive Tract

A number of bacteria, fungi, viruses, and protozoa can infect reproductive tissues, resulting in varying degrees of pathology ranging from little discomfort to death. The female reproductive tract has evolved innate and adaptive immune mechanisms that protect from microbial infection, thereby reducing infection and disease. Central to this

protection are the epithelial cells that line the female reproductive tract. In the uterus, columnar epithelial cells provide a physical barrier to microbial infection. In addition, epithelial cells produce chemokines and cytokines that attract and activate innate immune cells and serve as a link to the adaptive immune system. Further, uterine epithelial cells serve as a conduit for secretory antibodies to enter the lumen and can present antigen to T cells. These protective mechanisms contribute to an environment in the uterus that is generally considered sterile, unlike the environment in the lower female reproductive tract. The uterine environment is in constant flux due to the concentration changes in sex hormones that occur in preparation for reproduction. The sex hormones estrogen and progesterone alter the local immune system to prepare for conception, influence how well the immune system will tolerate antigenic sperm and a semi-allogeneic fetus and yet provide a network of protective immune mechanisms against microbial pathogens. Understanding how sex hormones influence uterine epithelial cell function will provide a basis for immune protection in the uterus.

Estrogen Effects on Immunity in the Female Reproductive Tract

Researchers examined the effects of sex hormones on immune-mediated responses of uterine epithelial cells. This study showed that estrogen inhibited the ability of uterine epithelial cells to respond to an inflammatory stimulus (IL-1), while progesterone had no effect. Estrogen limited the ability of uterine epithelial cells to produce antimicrobial peptides that protect the female reproductive tract from infection and also limited the production of chemotactic molecules that recruit immune cells to the site of infection. These results suggest that inflammatory responses may be reduced during ovulation and pregnancy. (*J. Immunology* 2005 175:6509-6516)

III. Related Accomplishments in Women's Health Research

A. Research Training and Career Development

Primary Caregiver Technical Assistance Supplements (PCTAS)

NIAID recognizes that postdoctoral scientists with young children or ailing parents may encounter barriers to career advancement when faced with the challenges of balancing the demands of research activities and primary caregiver responsibilities. As a result, productivity can be seriously compromised during this critical period of a young scientist's career. To support the career development of young investigators, NIAID has created the PCTAS program to provide technical support to postdocs who have primary caregiver responsibilities. Principal investigators with NIAID research grants are eligible to apply for technical support for a postdoctoral scientist for a period of 1-2 years. The program has been well received by the research community and three awards were made in the past two years.

Strengthening International AIDS Research on Women and Children

Through a NIAID sponsored grant on HIV Research in Women and Children, the University of Washington CFAR provided funds to eight international sites in Kenya, Mozambique, and Peru, based on a connective, peer-reviewed process, to strengthen these international sites conducting innovative HIV research on women and children. These include studies of mother-to-child transmission and HAART operational research, microbicide and prevention research, and vaginal infection research.

Mentoring International Investigators on HIV Research and Women's Health

The HIV and Women's NIAID sponsored grant at the Tufts University and Brown University CFAR has provided mentoring to international investigators on research related to HIV and women. Some of the services include: hands on training in gynecological collection methods and STD diagnosis and advice on establishing an HIV and women clinics, preparation and submission of grants, and implementation, analysis, and publication of research on HIV-infected women. The Core also helps mentor Brown University students, residents, and fellows interested in international work related to HIV and women in South Africa, Kenya, Cambodia, the Philippines, and Cape Verde.

B. Trans-NIAID Women's Health Research Workgroup

In 2006, NIAID established a trans-NIAID Women's Health Research Workgroup of NIAID staff to advise NIAID on matters pertaining to women and gender based research. The workgroup is focused on women's health and gender-based research activities that advance the mission and research priorities of NIAID, identify any gaps in research, and provide recommendations for future women's health research opportunities.

The programmatic goals of the workgroup are three-fold:

- To advise on the coordination of women and gender based research across the Institute.
- To develop a common framework for identifying and assessing women and gender based research.
- To encourage trans- NIAID and trans-NIH collaborations on women and gender based research activities.

IV. Initiatives

A. Initiatives in Topical Microbicide Research

1. Program Announcements

Integrated Preclinical/Clinical Program for HIV Topical Microbicides (IPCP-HTM)

A Program Announcement, co-sponsored with NICHD, entitled "**Integrated Preclinical/Clinical Program for HIV Topical Microbicides**" (IPCP-HTM) continued through 2006. The purpose of the PA is to stimulate iterative preclinical and clinical research for novel microbicide strategies against HIV infection. The overall goal is to encourage advanced optimization and development of new and pioneering topical microbicide candidates and combinations as well as to foster translation of new microbicides/combinations from preclinical studies to pilot clinical studies in order to segue these studies into large safety and efficacy clinical trials within the MTN. These three new awards made to Harvard Medical School, the Population Council and the Brown University will significantly expand the scope of the IPCP-HTM by introducing programs focusing on development of microbicides for HIV, HSV, and HPV and preclinical development of a triple combination microbicide.

In addition, previous awards were also proposed for competitive supplements. The competitive supplements were targeted to add specific functionality to the existing IPCP-HTM awards through Core funding. Two awards were made to University of California, Los Angeles and Starpharma, LTD., to develop and clinically evaluate a form of the microbicide formulated for rectal use. (PA-03-137)

2. Request for Applications

Microbicide Innovation Program (MIP)

NIAID, in coordination with the Office of AIDS Research (OAR), developed a new milestone-driven microbicide research program that was co-funded by Office of Research on Women's Health (ORWH) and cosponsored by NICHD and National Institute of Mental Health (NIMH). The focus of the program is to encourage: (1) discovery and exploration of microbicides (singly or in combination) directed against HIV or HIV and STIs linked to HIV acquisition; (2) emerging technologies or models that contribute to the development of new and/or more efficient methods of assessing microbicide safety, efficacy and acceptability; and (3) exploration of complex prevention strategies that incorporate microbicides with other modalities of prevention. Fifteen applications were identified for funding, 1 application was transferred to NIMH, 3 applications were transferred to NICHD, and 11 applications were proposed for NIAID funding. (RFA-AI-06-005)

Partnerships for Topical Microbicides Program

In FY 2005, through the Partnerships for Topical Microbicides program, NIAID made five awards that join industry and academic or other non-profit organizations together to develop and bring promising topical microbicide candidates from concept through pre-industry development to prepare them for clinical trials.

The focus of these partnership agreements is to develop a potential microbicide with a proposed dual indication, i.e., prevention of HIV and an STI, or prevention of two STIs. (RFA-AI-04-047)

3. Contracts

Specialized *In Vitro* Virological Evaluations of Strategies to Combat HIV/AIDS

The scope of the contract is to test compounds for their potential to be developed as topical microbicides in primary and secondary cell-based assays for their efficacy and safety. (N01-AI-05415)

The STD Prevention Primate Unit

The STD Prevention Primate Unit for preclinical evaluation of topical microbicides and vaccines at the University of Washington is being re-competed (RFP-07-18). An award is anticipated in 2007. This contract will evaluate microbicide candidates for safety (effects on surface tissues and microenvironment of the cervix and vagina) in pig-tailed macaques and for efficacy against STI pathogens. Results from this NIAID-supported testing contract are coordinated with other NIAID-funded testing to facilitate product development and safety and efficacy testing in clinical trials. (N01-AI-95388)

B. Initiatives in STI Research

Request for Applications

Improving Diagnostics Associated with Women's Health and Sexually Transmitted Infections

In 2002, NIAID established a series of grant programs to stimulate industry participation in the development of vaccines, drugs, and diagnostics for human infectious diseases of public health importance and products for controlling vectors that transmit infectious agents.

In 2005, the Partnerships to Develop Tools to Evaluate Women's Health was initiated to develop and evaluate a variety of tools and methods that will help define the complex ecosystem of the vaginal flora and pathogens in the context of immune response of the female reproductive tract. Specific areas of research include: assessing the vaginal ecology, measuring immune responses in the vagina, and assessing the influence of reproductive hormones on the vaginal ecosystem and the immune responses. Research also includes investigating the women's reproductive tract in both normal and altered physiological conditions.

During 2006, three companies were awarded grants through this partnership. They were Mattek Corporation (Investigating vaginal/cervical tissue models and endocrine effects and susceptibility to infection), the Institute for Genomics Research (Developing genomic tools for studying the ecology of the human vaginal microflora), and the Program for Appropriate Technology for Health (Developing a multiplex point-of-care test for vaginal infections). (RFA-AI-05-029)

C. Initiatives in Autoimmune Disease

1. Request for Applications

Autoimmunity Centers of Excellence (ACEs)

The nine Autoimmunity Centers of Excellence (RFA-05-026) conduct collaborative basic and clinical research on autoimmune diseases, including single-site and multi-site pilot clinical trials of immunomodulatory therapies and mechanism-of-action studies. The ACEs support close interaction between clinicians and basic researchers, which should facilitate the identification of effective tolerance induction and immune modulation strategies to treat or prevent disease and accelerate the translation of scientific advances to the clinic.

Clinical trials supported through the ACEs include:

- phase I/II clinical trial of anti-CD20 for treatment for lupus;

- phase I clinical trial of anti-TNF for treatment of lupus nephritis;
- phase I clinical trial of anti-CD20 for treatment of Sjogren's syndrome; and
- preclinical study of DNase treatment, now underway with a follow-on phase 1b trial planned.

Mechanistic studies supported through the ACEs include:

- study of immune responses against therapeutic anti-TNF molecules that could compromise their efficacy in rheumatoid arthritis; and
- analysis of regulatory T cells induced in patients treated with anti-CD3.

The ACEs are co-sponsored by the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) and the NIH ORWH. More information on the ACE is available on its website at

www.autoimmunitycenters.org. (RFA-AI-02-006)

The Autoimmune Disease Prevention Centers

The Autoimmune Disease Prevention Centers conduct research on the development of new targets and approaches to prevent autoimmune diseases and evaluates these approaches in pilot and clinical studies. In FY 2005, the Prevention Centers supported 22 pilot projects to test innovative approaches that may lead to the development of novel targets for disease prevention or assays for biomarkers of disease progression. (RFA-AI-05-026)

2. Contracts

Immune Tolerance Network (ITN)

The Immune Tolerance Network (ITN) is an international consortium of over 80 investigators in the United States, Canada, Europe, and Australia dedicated to the clinical evaluation of novel, tolerance-inducing therapies in autoimmune diseases, asthma and allergic diseases, and rejection of transplanted organs, tissues, and cells. The goal of these therapies is to "reeducate" the immune system to eliminate injurious immune responses and graft rejection while preserving protective immunity against infectious agents. To understand the underlying mechanisms of action of the candidate therapies and to monitor tolerance, the ITN has established state-of-the-art core laboratory facilities to conduct integrated mechanistic studies, and to develop and evaluate markers and assays to measure the induction, maintenance, and loss of tolerance in humans. Since its inception, the ITN has initiated more than 20 clinical protocols, over 15 state-of-the-art core laboratory facilities, and over 10 additional studies designed to explore immune mechanisms leading to the development, maintenance, or loss of clinical tolerance. Currently, the ITN supports seven clinical trials in solid organ and islet transplantation and two cohort studies to understand the immune mechanisms involved in the acquisition of spontaneous tolerance to organ grafts. The ITN, co-sponsored by the NIDDK and the Juvenile Diabetes Research Foundation International (JDRF). More information on the ITN is available on its website at www.immunetolerance.org. (RFP-AI-04-44)

The Multiple Autoimmune Diseases Genetics Consortium (MADGC)

The Multiple Autoimmune Diseases Genetics Consortium is a repository of genetic and clinical data and specimens from families in which two or more individuals are affected by two or more distinct autoimmune diseases. This repository provides well-characterized genetic material on 363 families for use in research aimed at identifying the genes involved in autoimmune diseases. Samples from 1,243 affected individuals and approximately 1,000 control subjects, all with associated clinical information, are available to qualified researchers. More information can be found at <http://www.madgc.org>. (RFP-AI-99-30)

D. Initiatives on Sex Based Differences in the Immune Response

1. Request for Applications

NIAID, in collaboration with National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), National Institute of Neurological Disorders and Stroke (NINDS), ORWH, and the National Multiple Sclerosis Society, supports the "Sex Based Differences in the Immune Response" research initiative. In addition, NIAID, with the NIH OAR and the NIH ORWH, support a program project to investigate the differences in the immune response in the female reproductive mucosa. While differences in the immune response of males and females have

been documented, including the increased incidence of autoimmune diseases in women, the reasons for pregnancy-induced changes in immune mediated diseases, and differences in the rate and severity of disease are unclear. Increased understanding of the mechanisms underlying the differences in the immune response in males and females should allow more targeted approaches for the prevention and treatment of immune-mediated disease. (RFA-01-005)

D. Conferences and Workshops

Workshop on Self-obtained Vaginal Swabs for Diagnostic Testing

A workshop was held in June 2006, in Bethesda, MD, to present published data on self-obtained vaginal swabs for diagnostic testing. Representatives from FDA, Centers for Disease Control and Prevention, and NIH attended the workshop along with investigators and companies involved with *in vitro* diagnostics. Active dialogue among conference participants may lead to future collaborations.

Workshop on Regulation of Inflammatory Responses: Influence of Sex and Gender

On September 19-20, 2006, the NIH ORWH and the NIAID convened a workshop on the influence of sex and gender on the regulation of inflammatory responses. Investigators from the United States and Europe presented their research findings and provided participants with a state of the science. Representatives from across the NIH attended the workshop, including representatives from the National Cancer Institute; the National Heart, Lung and Blood Institute ; National Institute of Aging; the National Institute on Alcohol Abuse and Alcoholism; the NIAMS; the NICHD; the National Institute of Dental and Craniofacial Research ; the National Institute of Drug Abuse; the National Institute of General Medical Sciences; the NIMH; and the NINDS. The initial session provided a basic foundation of what inflammation is, and subsequent sessions explored sex differences in the burden of disease and response to insult, cellular and molecular mechanisms in inflammation, and emerging strategies to treat inflammatory disease. Presentations were followed by discussions in which workshop participants identified gaps in knowledge, research needs, and opportunities for future research. Recommendations for research opportunities will be incorporated into a trans-NIH initiative on inflammation.

Workshop on Development of Standardized Microbicide Toxicity Tables for Clinical Trials

NIAID staff organized a workshop entitled "Development of Standardized Microbicide Toxicity Tables for Clinical Trials". The toxicity tables will be used in NIH-sponsored vaginal and rectal microbicide trials, as well as those sponsored by other agencies. Participants included interested stakeholders from NIH, FDA, industry and other funding agencies. The workshop was held Nov. 2-3, 2006 in the Washington, D.C. area.

World AIDS Day conference on Women's Health

The **CFAR at Harvard University** participated in the conference, "World AIDS Day: Living our Lives" - A World AIDS Day conference on Women, which was held on December 1, 2005. This conference, which was held at University of Massachusetts-Boston, was organized by a multi-agency planning committee and drew more than 150 attendees. The conference included a range of topics, such as sessions on domestic violence, addiction, and women's health concerns, as well as a vendor fair that provided resources and information to participants about local community organizations.

Forum on Lipodystrophy Conference

The **University of California, San Diego CFAR** was involved in organizing a community medical update of information presented at the Lipodystrophy Conference in January 2005. An HIV and clinical trials overview was given to HIV-infected English speaking women in February 2005, and to HIV-infected Spanish speaking women in September 2005.

HIV and Women: The Female Face of the Epidemic

The **University of Washington CFAR** held a Mini-Symposium: "HIV and Women: The Female Face of the Epidemic" on October 4, 2005, that was attended by more than 100 faculty members, students, and HIV activists. This **CFAR** developed a course on HIV and women that has expanded over the past year and a half into a new

Graduate Certificate Program in HIV and STIs. The comprehensive curriculum addresses the complex interplay of biomedical, social, economic, gender, political and geographic factors that impact the spread and disease course of HIV and STIs.

Key Note Address at the Caribbean Women’s Health Association’s World AIDS Conference

NIAID staff presented the key note address entitled, “The Impact of HIV and AIDS on the African American and Caribbean Women in the United States” at the Caribbean Women’s Health Association’s World AIDS Day 2006 conference in Brooklyn, New York. Findings from the NIAID-sponsored Women’s Interagency HIV Study were presented at this conference. Over 100 health professionals attended this event.

Women in Science Workshop on International Research Opportunities in Infectious Disease for New Investigators

NIAID staff presented a workshop on funding opportunities for international investigators at the Second International Conference on Women and Infectious Diseases, which held in Atlanta, Georgia in March, 2006. Information on the NIAID-sponsored Comprehensive International Program of Research on AIDS (CIPRA) was presented to investigators from Africa, Asia and Latin America.

Forum on the First National Women and Girls HIV/AIDS Awareness Day

Dr. Betsey Harold, a NIAID-sponsored scientist, gave the inaugural address , at the first national Women and Girls HIV/AIDS Awareness Day, entitled, “Women and Girls HIV/AIDS Awareness Day: A Life Cycle Perspective” held at the Lipsett Amphitheater on March 10, 2006. She spoke about the NIAID-sponsored microbicide research program. Over 200 NIH staff participated in this event.