MINORITY AND WOMEN'S HEALTH

The Office of Special Populations and Research Training (OSPRT) provides oversight and coordination to NIAID's activities in the area of minority and women's health. OSPRT has provided the National Center for Minority Health and Health Disparities with benchmarks on progress made to initiatives contained in the NIAID fiscal year (FY) 2002–2006 *Strategic Plan on Health Disparities.* The plan comprises three goals: (1) to conduct research to identify and address health disparities among various populations affected by infectious and immunologic diseases, (2) to increase the number of minority scientists and grantees, and (3) to improve education and outreach activities for the transfer of health information to these populations. NIAID continues to prioritize basic, clinical, and epidemiologic research on these health problems; efforts to increase participation of minority scientists in its research; and outreach activities designed to communicate research developments to these populations. The plan is available online at the following NIAID Web site: *www.niaid.nih.gov/healthdisparities/niaid_hd_plan_final.pdf.*

OSPRT staff played a major role in updating the NIH *Report on Monitoring Adherence to the NIH Policy on the Inclusion of Women and Minorities as Subjects in Clinical Research (www4.od.nih.gov/orwh/inclusion.html)* as required by the Government Accounting Office. OSPRT staff also assisted in the development of the *Outreach Notebook* for extramural principal investigators who conduct or plan to conduct clinical trials with human subjects. This document can be accessed at *www4.od.nih.gov/orwh/outreach. pdf.*

Minority Health

Asthma is a chronic disease affecting more than 14 million Americans; it disproportionately affects minorities, particularly African-American and Hispanic children residing in inner cities. Preliminary results from the Inner-City Asthma Study, co-sponsored by the National Institute of Environmental Health Studies (NIEHS), indicate that physician education and an extensive environmental intervention successfully reduced asthma symptoms among inner-city children, and continue to do so 1 year post-intervention. The environmental intervention resulted in several weeks of additional symptom-free days, a reduction in unscheduled medical visits, and improvements in asthma symptoms correlated with reductions in home allergen levels. The physician feedback intervention resulted in a 20-percent decrease in unscheduled emergency room or clinic visits for poorly controlled asthma. These findings should lead to significantly improved health for inner-city children with asthma and reduce the high medical, economic, and social costs associated with this disease.

Organ transplantation represents a key health disparity for African Americans. It has been shown that African Americans are less likely to be identified as candidates for renal transplantation or to find a suitable donor and tend to remain longer on transplant waiting lists. There is a lower organ donation rate among African Americans than among other racial groups, although African Americans comprise approximately 35 percent of patients on the renal transplant waiting list.

Successful transplantation depends on the availability of donated organs and accurate

methods to match donor and recipient human leukocyte antigen (HLA) types. Recognizing that knowledge of the relevant HLA types in minority populations is incomplete, NIAID supports efforts to improve the definition of ethnically restricted HLA genes. These efforts have contributed to reducing incomplete tissue matching for transplant recipients. NIAID supports demonstration and education projects in Louisiana and Washington to increase organ donation awareness among minority populations through a variety of community outreach approaches.

Autoimmune diseases are those in which the immune system mistakenly attacks the body's own cells, tissues, and organs. Autoimmune diseases affect an estimated 5 to 8 percent of the U.S. population. Several of these diseases, such as systemic lupus erythematosus (SLE) and scleroderma, disproportionately affect women and minority populations. NIAID supports a broad portfolio of basic, preclinical, and clinical research aimed at understanding the pathogenesis of autoimmune diseases, investigating new ways to modify the immune system, and applying this knowledge to identification and evaluation of promising approaches to treat and prevent these diseases. These programs include the Autoimmunity Centers of Excellence and the Autoimmune Diseases Prevention Centers. NIAID also supports multidisciplinary research targeting the identification, characterization, and definition of sex-based differences in the immune response. In 2002, the NIAID-chaired NIH Autoimmune Diseases Coordinating Committee published its plan for autoimmune diseases research. This plan can be found at *www.niaid.nih.gov/dait/pdf/ADCC_Report.pdf.*

Collaborations among NIAID, the National Institute of Diabetes and Digestive and Kidney Diseases, and the Juvenile Diabetes Research Foundation International established the Immune Tolerance Network (ITN), an international consortium dedicated to the clinical evaluation of novel, tolerogenic approaches for the treatment of autoimmune diseases, asthma, and allergic diseases, and the prevention of graft rejection. ITN also conducts integrated studies on the underlying mechanisms of these approaches and develops and evaluates markers and assays to measure the induction, maintenance, and loss of tolerance in humans. ITN includes more than 80 basic and clinical scientists and physicians at more than 40 institutions in the United States, Canada, Europe, and Australia.

Hepatitis C virus (HCV) infection is the most common chronic blood-borne viral infection in the United States. Various surveys indicate that HCV disproportionately affects minority populations. Moreover, available treatments for HCV tend to be less effective for African Americans than for other populations. To investigate this issue, NIAID is supporting a study to determine whether there are specific genetic and molecular factors that cause African-American patients to respond poorly to the standard interferon and ribavirin therapy used for hepatitis C that seems to be effective in white populations. Understanding the reasons for differential drug responses among these populations may lead to new HCV-targeted drugs. In another study supported by NIAID, researchers are studying the effect of repeated exposures to hepatitis C through needle sharing in a cohort of intravenous drug users in urban settings. The study showed that subjects with previous exposure to HCV were more able to fight off secondary infections than were subjects who had never had exposure to HCV. These findings suggest that humans can acquire immunity that protects

against disease caused by HCV. Other NIAID-supported researchers demonstrated that specific immune cell responses can be identified that resulted in clearance of infection and demonstrated different ways the virus becomes persistent in chronic carriers. NIAID-supported scientists also demonstrated that the outcome of hepatitis C infection could be predicted on the basis of the viral mutations that allow the virus to escape discovery.

It is estimated that one-third of the world's population (1.86 billion) is infected with the bacterium that causes tuberculosis (TB) and that 16.2 million people currently have active TB disease worldwide. There are approximately 2 million TB cases per year in sub-Saharan Africa, 3 million in Southeast Asia, and 250,000 in Eastern Europe. The global incidence rate of TB is growing at approximately 0.4 percent per year. TB also remains a public health concern in the United States. It is estimated that 10 to 15 million people in the United States currently are infected with this pathogen,[44] with 15,989 new TB cases reported in the United States in 2001.[45] The increasing spread of this disease continues to be a public health challenge in the industrialized world because of several forces: increases in urban poverty and prison populations, injection drug use, and increasingly crowded housing and long-term care facilities. These combined factors also may contribute to the disproportionate impact of TB on minority populations. During 2002, approximately 75 percent of the reported active TB cases in the United States were among foreign-born persons and U.S.-born non-Hispanic African Americans. Data from 2000 also showed that seven southeastern States (not including Florida and Texas) bear a disproportionate burden of TB disease. The rise of multidrug-resistant strains and co-infection of TB with HIV/AIDS has further extended the impact of TB on various populations in the United States and around the world.

Over the past decade, dramatic increases in NIAID funding for TB research have allowed the Institute to support a wide range of TB initiatives and to increase the community of TB researchers. In FY 2003, a contract under the "Millennium Vaccine Initiative—Novel Vaccines for TB and Malaria" was awarded to the Corixa Corporation for the development of new vaccines for use in developing countries. NIAID also supports international clinical studies of TB/HIV co-infection, with active Institute program staff participation on projects in Africa, Asia, and South America. NIAID continues to support the Tuberculosis Research Unit at Case Western Reserve University, which conducts multidisciplinary laboratory and clinical studies to answer critical questions in human TB; provides knowledge, tools, and technologies to improve clinical trials in TB; and offers the ability to conduct clinical studies for the evaluation of new or improved vaccines, therapeutics, and diagnostics *(www.tbresearchunit.org)*. A high-priority goal is the development of improved TB vaccines. Through the TB research materials and vaccine-testing contract, NIAID provides TB research reagents and offers testing services for vaccine candidates in animals to qualified investigators throughout the world.

Sexually transmitted infections (STIs) are critical global and national health priorities because of their devastating impact on women and infants and their causal association with HIV infection. STIs are widespread, with 15 million new cases estimated to occur each

year in the United States.[46] While the number of cases of STIs between 1997 through 2000 decreased in African Americans by 41 percent, the number of cases increased for Hispanics by 12.5 percent. Several STIs, including gonorrhea, chlamydia, and syphilis, have higher incidences among minorities than among whites in the United States.

NIAID supports research for more effective prevention and treatment approaches to the control of STIs. In November 2002, a public-private partnership between NIAID and GlaxoSmithKline supported the launch of the Herpevac clinical trial, a phase III double-blind clinical efficacy trial of an investigational vaccine for the prevention of genital herpes. In previous, smaller trials the vaccine being tested has been shown to be effective only in women, suggesting that the vaccine may be working in part by providing mucosal immunity (antibody protection in the mucous membranes such as the respiratory, gastrointestinal, and reproductive tract). The study will enroll 7,550 women at approximately 25 sites across the United States. If this vaccine is found to be effective, it would provide a new means for preventing this disease, whose estimated prevalence in the general U.S. population aged 14 to 49 years is 19 percent. Another NIAID-supported clinical trial currently in development will study the effectiveness of the diaphragm in preventing chlamydia and gonococcal infection at three clinical sites in Madagascar. The Institute's ongoing efforts include the STI Cooperative Research Centers, the STI Clinical Trials Unit, and the Topical Microbicides Program projects. In addition, NIAID continues to initiate and support a variety of other research projects that focus on (1) developing vaccines, topical microbicides, and treatments for the microbes that cause STIs; (2) developing better and more rapid diagnostics; (3) sequencing the genomes of sexually transmitted pathogens; and (4) understanding the long-term health impact of sexually transmitted pathogens in various populations.

AIDS continues to disproportionately affect minorities. Racial and ethnic populations in the United States, primarily African Americans and Hispanics, constitute 57 percent of the more than 800,000 cases of AIDS reported to the Centers for Disease Control and Prevention (CDC) since the epidemic began in 1981. African Americans make up almost 38 percent of all AIDS cases reported in the United States, yet according to the U.S. Census Bureau, they comprise only 12 percent of the U.S. population. Hispanics represent 18 percent of all AIDS cases and are approximately 13 percent of the U.S. population. Of the new AIDS cases reported in 2001, 49 percent were among African Americans, 20 percent among Hispanics, 30 percent among whites, and less than 1 percent among American Indians/Alaska Natives and Asian Americans/Pacific Islanders. Among women, African Americans and Hispanics account for 78 percent of AIDS cases; among men, African Americans and Hispanics account for 52 percent of cases. Injection drug use is a major factor in the spread of HIV in minority communities. Other factors contributing to the spread of HIV/AIDS in these communities include men who have sex with men (MSM) and, increasingly, heterosexual transmission.

One of the greatest challenges facing AIDS researchers today is the recruitment and retention of minorities for clinical trials. As the epidemic expands into minority communities, inclusion of these individuals in

clinical trials is particularly urgent to ensure that the results of research are applicable to all populations affected by the disease. To address this issue, NIAID released a new program announcement (PA), titled "Enrolling Women and Minorities in HIV/AIDS Research Trials," to fund innovative approaches to reach, enroll, and retain women and racial/ethnic minorities in HIV/AIDS research trials in the United States. The PA will support projects to increase the number of women and minorities who participate in clinical trials for HIV/AIDS, relative to the incidence data, and advance the body of scientific knowledge that will improve the diagnosis, treatment, and development of preventive strategies in women and minorities.

Each of NIAID's large, multicenter therapeutic clinical trials networks, namely, the Adult AIDS Clinical Trials Group (AACTG), the Terry Beirn Community Programs for Clinical Research on AIDS (CPCRA), and the Pediatric AIDS Clinical Trials Group (PACTG), strives to ensure enrollment of a sufficient proportion of minority subjects.

NIAID's epidemiologic research explores the clinical course and factors contributing to transmission of HIV infection in a variety of populations. Groups of inner-city women and their children are the focus of the Women and Infants Transmission Study (WITS), and the Women's Interagency HIV Study (WIHS) includes both HIV-infected and uninfected women. The Multicenter AIDS Cohort Study (MACS) is a prospective, longitudinal study of HIV disease in homosexual and bisexual men. WIHS and MACS are the two largest observational studies of HIV/AIDS in women and homosexual or bisexual men, respectively, in the United States. Studies from these cohorts have repeatedly made major contributions to understanding how HIV is spread, how the disease progresses, and how it can best be treated. WIHS and MACS have completed their expansion to increase the size of the study groups by 60 percent and increase the number of minority participants. The expanded cohorts will focus on contemporary questions regarding HIV infection and treatment.

The HIV Vaccine Trials Network (HVTN) is an international network dedicated to developing HIV vaccines through testing and evaluating candidate vaccines in clinical trials. The HIV Prevention Trials Network (HPTN) is an international network dedicated to conducting clinical trials of nonvaccine HIV prevention strategies, including topical microbicides and mother-to-child transmission (MTCT) studies to develop and evaluate simple and less costly prevention regimens suitable for global use. MTCT studies also are carried out in PACTG. Both HVTN and HPTN have initiated community outreach programs to educate people about HIV vaccine and prevention research and to encourage participation in clinical trials. Through these outreach activities, HVTN and HPTN hope to enroll a diversified population in their clinical trials, with an emphasis on recruiting minorities and women.

NIAID is currently in year 2 of its HIV Vaccine Communications Campaign, which is developing and implementing a national campaign to increase awareness of and support for HIV vaccine research, especially in at-risk populations. NIAID receives input and guidance for developing appropriate and culturally sensitive messages from its HIV Vaccine Communications Steering Group, which consists of representatives from

community groups, other Government agencies, pharmaceutical companies, and HIV vaccine advocacy groups. A national survey was completed this past year in which the attitudes toward and knowledge of HIV vaccine research were evaluated in the general population as well as in segmented groups of African Americans, Hispanics, and MSMs. Key findings of the survey indicate that large segments of African Americans and Hispanics believe that an HIV vaccine already exists and is being kept secret, did not know that vaccine trial volunteers have to be HIV negative, and did not know that you cannot get HIV from the vaccines being tested. The campaign is working to correct these misconceptions and to provide general information about HIV vaccine research. For more information, visit *www.niaid.nih.gov/newsroom/mayday/default.htm.*

An additional challenge is the recruitment of underrepresented minority investigators to AIDS and AIDS-related clinical and basic research disciplines. To address this challenge, NIAID supports a comprehensive portfolio of biomedical and behavioral research aimed at preventing and treating HIV disease in minority communities, training minority investigators, and fostering infrastructure development. NIAID continues to co-fund, with the National Center for Research Resources, the Research Centers in Minority Institutions (RCMIs) program by providing support for HIV/AIDS research pilot projects as well as infrastructure development at RCMIs. In FY 2003, NIAID awarded projects to eight institutions for research in diverse areas such as clinical, molecular, and vaccine development; drug development; opportunistic infections; and immunology. In addition, NIAID awards grant supplements under the Research Supplements for Underrepresented Minorities (RSUM) program. The purpose of RSUM is to attract underrepresented minority investigators into biomedical and behavioral research. The supplements are made to NIAID-funded grantees to recruit and support investigators interested in a particular area of scientific research. The awards are made on behalf of postdoctoral candidates, graduate students, faculty members, undergraduates, and reentry and disabled investigators. Several of the NIAID-sponsored Centers for AIDS Research (CFARs) also have a significant commitment to educating and training minority investigators and providing outreach to minority communities.

One of the greatest challenges facing AIDS researchers is the recruitment and retention of minorities for clinical trials. As the epidemic expands into minority communities, inclusion of these individuals in clinical trials is particularly urgent to ensure that the results of research are applicable to all populations affected by the disease. To this end, NIAID hosted a conference to explore what works in the recruitment of minorities and women. The conference, titled "Increasing Diversity in Clinical Trials: Best Practices" *(www.orau.gov/hdsymposium/default.htm),* was held October 2, 2003, and was attended by 200 individuals from academia, private industry, and community-based organizations.

Minority Researchers' Training and Enhancement Programs

Increasing the participation of underrepresented minority investigators in virtually all fields of biomedical research is a continuing NIH and NIAID priority. In addition to supporting NIH-wide programs, NIAID has developed and supported a variety of innovative minority programs for

biomedical research, encompassing high school through postdoctoral training.

In February 2003, NIAID launched an extramural arm to its longstanding Introduction to Biomedical Research Program. The Richard M. Asofsky Scholars In Research (ASIR) program was created to represent and honor Dr. Asofsky's dedication to bringing underrepresented minorities into the biomedical sciences. The ASIR program provides supplemental funding to NIAID extramural principal investigators for the purpose of supporting underrepresented minority high school and college students in their research laboratories and to expose them to research career opportunities in the areas of allergy, immunology, transplantation, microbiology, and infectious diseases, including AIDS. These NIAID ASIR awards are used to encourage the development of underrepresented minority researchers as outlined in the NIAID *Strategic Plan on Health Disparities.* Information on who is eligible to apply and other requirements for the supplement can be found at the following site: *http://grants2.nih.gov/grants/guide/pa-files/PAR-03-071.html.* For FY 2003, 15 students were supported by 5 NIAID grantees.

In July 2003, NIAID announced an initiative that solicits applications from underrepresented minority investigators who are in the early stages of their scientific careers (assistant professor or junior-level faculty) to establish basic or clinical research programs in the areas of allergy, immunology, transplantation, microbiology, and infectious diseases, including AIDS. The goals of the program are to increase the number of underrepresented minority investigators performing independent competitive research in the areas encompassed by NIAID's scientific mission and to enhance the long-term research skills and potential of these individuals. Information on the NIAID Enhancement Awards for Underrepresented Minority Scientists initiative is located at *http://grants1.nih.gov/grants/guide/rfa-files/RFA-AI-03-045.html.*

Since 1993, NIAID had conducted a symposium designed for recipients of the Research Supplement for Underrepresented Minorities to encourage them to remain in the biomedical research agenda of NIAID. In November 2003, NIAID plans to hold its sixth Bridging the Career Gap for Underrepresented Minority Scientists symposium.

NIAID's Division of Intramural Research (DIR) Office of Training and Special Emphasis Programs (OTSEP) launched a new outreach program for minorities—Intramural NIAID Research Opportunities (INRO), in April 2003. This 4-day program will be offered annually and includes scientific lectures by NIAID researchers, discussions with scientists, and tours of the Research Technology Branch and the Vaccine Research Center. Three key features distinguish this new program and will result in more minority students participating in intramural training programs at all levels and, eventually, create a large pool of potential candidates for career positions in NIAID. First, the selection of students will be based on academic excellence, interest in NIAID research, and desire to participate in NIAID's DIR training programs. Second, current DIR minority trainees will be included in all aspects of the program, to include giving presentations. This aspect will allow the visiting students to see firsthand what can be accomplished and to network with the trainees. Third, all

participants will be tracked in future years to inform them about NIAID training and professional opportunities and to enlist their participation in OTSEP's outreach activities. Eleven outstanding students were selected from a nationwide pool to attend the first INRO, and 25 DIR minority trainees participated. The visiting students, DIR trainees, and faculty all rated the program as excellent. Six INRO participants were selected to participate in NIAID's summer internship program, and one was selected to participate as a postbaccalaureate. Those INRO students in graduate school will be recruited for postdoctoral positions in the coming years. As a result of the success of the first offering of INRO, the number of interns selected for INRO 2004 will be increased, and the program will be lengthened by 1 day.

OTSEP Underrepresented Minority Programs were expanded in 2003, with the sponsorship of 13 postbaccalaureate Intramural Research and Training Awardees (IRTAs), 2 postdoctoral IRTAs, and 6 NIH Academy students. Several programs were conducted for these trainees, including a new Brown Bag Lunch series, which gave the trainees an opportunity to speak informally with senior NIAID scientists. Seven OTSEP-sponsored trainees, having completing their second postbaccalaureate year in NIAID, entered graduate or medical schools such as Albert Einstein School of Medicine, Emory Medical School, Georgetown University School of Medicine, Harvard Medical School, Tri-institutional Medical School—Cornell/Rockefeller/Sloan-Kettering, University of Maryland Medical School, and Washington University. OTSEP will continue to track the careers of these talented young scientists and inform them of additional training opportunities in NIAID.

Women's Health

A number of diseases affect women at a disproportionately high rate. To ensure the appropriate representation of women and minorities in clinical research studies of these and other diseases, the NIH Revitalization Act of 1993 (Public Law 103-43) established specific guidelines for the inclusion of women and minorities in all NIH-funded clinical research. These guidelines help ensure that valid analyses of differences in intervention effects can be conducted; they also provide the impetus for outreach efforts to recruit these groups into clinical studies.

Many infectious, immunologic, and allergic diseases affect women at high rates and fall under the mandate of NIAID. The Institute conducts research, either through its own laboratories or through funded mechanisms, on a broad spectrum of these diseases. The majority of NIAID's clinical studies on HIV/AIDS, autoimmune diseases, chronic fatigue syndrome, and STIs involve women.

Worldwide HIV/AIDS continues to increase among women. By the end of 2002, the Joint United Nations Programme on HIV/AIDS estimated that 19.2 million women were living with HIV/AIDS worldwide, accounting for nearly 50 percent of all cases.

In the United States, as of December 2001, women accounted for approximately 17 percent (141,048) of the 816,149 AIDS cases reported among adults and adolescents. Another 4,413 cases were reported in girls aged 13 years and younger. In recent years, the incidence of AIDS increased more rapidly among women than men. The proportion of new AIDS cases among women more than tripled from 1985 to 2001—from 7 percent to 26 percent.

Thirty-nine percent of HIV-infected women in the United States acquired HIV through heterosexual contact with HIV-infected men and 17 percent through injection drug use. HIV infection also disproportionately affects minority women. Seventy-six percent of HIV-infected women are African American and or of Hispanic ethnicity, compared with only 56 percent of HIV-infected men.

NIAID researchers are conducting numerous studies of HIV and women and continue to make discoveries that shed light on the nature of HIV infection. NIAID is studying the unique features of HIV/AIDS in women through two cohort studies, WIHS and WITS. WIHS is a multicenter prospective cohort study established in August 1993 to study the natural history of HIV infection in women. It conducts focused investigations of clinical, laboratory, and psychosocial aspects of HIV infection in women. WITS studies the pathogenesis of disease progression in women and children in an era of highly active antiretroviral therapy (HAART) and evaluates the factors related to perinatal HIV transmission and disease progression in women and children. In addition, NIAID supports clinical research on gender-specific differences and issues in disease progression, complications, treatment, and prevention strategies through several large clinical trials networks—AACTG, PACTG, CPCRA, and HPTN.

In the past, WIHS researchers examined factors associated with an increased risk of HIV transmission and the impact of HAART. These studies showed that HIV infection and the use of antiretroviral therapy (ART) were not associated with changes in menstrual cycle. Recently, however, WIHS studies have looked at menstrual cycles and how substance abuse, psychotherapeutic medications, alcohol or tobacco consumption, and the use of marijuana or crack cocaine were or were not associated with menstrual irregularities. Only the use of psychotherapeutic medications was found to affect the odds of having either a very short or a very long cycle. These findings emphasize the need for clinicians to take into consideration whether or not non-HIV-related medications are being used when evaluating menstrual disruptions in HIV-infected women.

Another WIHS study published this year found that the incidence of type 2 diabetes was significantly higher among women who used protease inhibitors compared with those receiving reverse transcriptase inhibitors, those not on any ART, and uninfected women. These results suggest that routine diabetes screening should be considered, especially among heavier and older women who are using protease inhibitors and who are from populations already at an increased risk of type 2 diabetes.

WIHS researchers also conducted a study of 204 HIV-infected women to determine whether C-reactive protein, an inflammatory marker, might serve as a low-cost way to help evaluate HIV disease progression in women. (Research has previously shown that high levels of C-reactive protein predict a poorer prognosis for other diseases such as atherosclerosis, renal disease, and cancer.) In this study, WIHS researchers found that higher C-reactive protein levels were associated with a higher risk of death in this specific population of HIV-infected women. This finding suggests that C-reactive protein may be a useful and inexpensive predictor of HIV disease mortality in women.

Mother-to-child transmission (MTCT) of HIV—which can occur during pregnancy or childbirth or through breastfeeding—accounts for more than 90 percent of all cases of childhood HIV infection, especially in countries where effective ARTs are not available.

According to the Centers for Medicare & Medicaid Services *(http://cms.hhs.gov/hiv),* of the 18 million women eligible for Medicaid in the United States, approximately 32,000 are infected with HIV; of those, about 3,000 are pregnant. Virtually all new infections in children are transmitted perinatally. As more women of childbearing age become infected, the number of children infected with HIV also is expected to rise. Efforts to prevent MTCT by targeting both the infant and the mother are being examined by both HPTN and PACTG, two NIAID-funded networks that support both domestic and international clinical research.

This year, follow-up data from an NIAID-funded study that began in November 1997 in Uganda found that the initial benefit to infants who, along with their mothers, received one dose of nevirapine (NVP), was sustained by the group of children until they reached age 18 months. Few serious side effects were attributable to NVP. Approximately 99 percent of the study participants breastfed their children; after 18 months, most of the women had completed breastfeeding, with the average duration lasting 9 months. This reduction in risk is consistent with the 42-percent risk reduction that was found when these infants were aged 6 to 8 weeks. The findings offer compelling new evidence that short-course NVP effectively and safely reduces MTCT of HIV and, because of its low cost and ease of administration, provides an important alternative in resource-poor developing countries. A final follow-up study will be conducted in 2004 when the children are aged 5 years.[47]

NIAID continues to support other research on gender-specific issues in HIV treatment through AACTG. A number of studies have been initiated through AACTG to examine, among other research questions, the pharmacokinetics of contraceptives in the setting of HAART; the use of ART in pregnancy; gender differences in responses to HAART among treatment-naive patients; toxicities and complications of different treatment regimens for HIV and HIV co-infections, such as human papillomavirus (HPV); metabolic complications of HAART; and changes in immunologic responses during postpartum.

NIAID has taken the lead on autoimmune disease research, another health issue that disproportionately affects women. Autoimmune diseases are chronic, disabling disorders in which underlying defects in the immune response lead the body to attack its own organs and tissues. More than 80 autoimmune diseases have been identified. Collectively, autoimmune diseases are thought to affect approximately 14 to 22 million people in the United States and disproportionately afflict women. In some autoimmune diseases, including thyroiditis, scleroderma, systemic lupus erythematosus, and Sjögren's syndrome, females represent 85 percent or more of patients. Ninety percent of the nearly 2 million Americans diagnosed with (or suspected of having) SLE are women. SLE damages multiple tissues and organs and may affect muscles, skin, joints, and kidneys as well as the brain and nerves. In other diseases such as multiple sclerosis, myasthenia gravis, and inflammatory bowel

diseases the disparity is smaller, with females representing 55 to 70 percent of patients. The reasons for these sex-based variations are not known. NIAID's Division of Allergy, Immunology, and Transplantation (DAIT) supports a broad range of basic and clinical research programs in autoimmunity, including programs to elucidate the genetics of autoimmunity and sex-based differences in the immune response. DAIT also supports the Autoimmunity Centers of Excellence (ACEs) to foster collaborative basic and clinical research on autoimmune diseases, including single-site and multi-site pilot clinical trials of immunomodulatory therapies *(www.niaid.nih.gov/dait/pdf/ADCC_Report.pdf).*

An estimated 15 million new cases of STIs occur in the United States each year. Although some STIs (e.g., syphilis) have declined to all-time lows, others (e.g., genital herpes, gonorrhea, and chlamydia) continue to spread through the population, posing a significant public health problem. Since symptoms in women are minor or nonspecific, especially in the early stages, STIs in women sometimes are not diagnosed until late in the disease. STIs that occur during pregnancy also can affect the fetus or newborn. About one-quarter to one-half of women infected with an STI during pregnancy give birth to either premature or low-birthweight infants. In about one-third to two-thirds of these pregnancies, the infection is passed to the infant and may cause permanent disabilities. Chlamydia, gonorrhea, and other infections of a woman's upper reproductive tract also can complicate pregnancy.

NIAID's multidisciplinary research strategy to address the complications of STIs includes basic science, vaccine development, behavioral science, development of topical microbicides, and development of rapid and inexpensive diagnostic tests. As research increasingly connects the risk of HIV transmission to the presence of STIs, NIAID has continued research into the biological, biochemical, and behavioral basis of various STIs as well as their manifestations and potential treatments. NIAID supports STI research through grants to individual investigators, a variety of research programs, STI Cooperative Research Centers, the Institute's STI Clinical Trials Unit, and NIAID's Topical Microbicides Program projects. NIAID is taking both preventive and therapeutic approaches to STIs in clinical trials. One example of a prevention trial that NIAID is currently planning is a trial at three clinical sites in Madagascar to study the effectiveness of the diaphragm in preventing chlamydia and gonococcal infection.

An estimated 3 million new infections of *Chlamydia trachomatis* occur each year. Investigators at NIAID's Rocky Mountain Laboratories are studying the immune response to chlamydial infection and are conducting preclinical testing of candidate vaccines. In addition, NIAID scientists and their collaborators implemented routine screening for the prevalence and risk factors for chlamydial infection among U.S. Army recruits. Among 23,010 female Army recruits, chlamydia prevalence was 9.51 percent for 4 years. Risk factors for infection included African-American ethnicity, young age (< 25 years), southern U.S. residence, more than one sex partner, a new sex partner, and history of any sexually transmitted infection. The finding of sustained high rates of *C. trachomatis* infection in this population provides justification and support for a chlamydia-control program for young women entering the Army.

About one in five adults in the United States has genital herpes, but only one-third of those people know they have the virus. Although most genital herpes cases present no symptoms, asymptomatic individuals can transmit herpes simplex virus (HSV) to others, and a pregnant woman infected with HSV can transmit the virus to her baby. Between 20 and 60 percent of U.S. women of childbearing age have been infected with genital herpes, posing a significant risk of neonatal herpes. NIAID currently is investigating prevention methods, including antiviral drugs, monoclonal antibodies, and vaccines. Because about 45 million to 60 million people in this country have genital herpes, these studies are important to assess the role of antiviral suppressive therapy in decreasing herpes transmission. The evaluation of monoclonal antibodies as part of a concomitant therapeutic regimen for babies with neonatal HSV infection also could help battle the persistent problem of neonatal herpes, which is still a life-threatening infection despite the availability of antiviral therapies.

At any one time, an estimated 20 million people in the United States have genital HPV infections that can be transmitted to others. Studies show high levels of HPV infection in women, with the highest levels in the younger age groups.

Although sexual activity is the most common way to transmit syphilis, pregnant women with the disease can pass the bacterium to their unborn children, which may cause serious mental and physical problems. NIAID is currently supporting a clinical research protocol examining a single oral dose of therapy for early syphilis. The goal of the study is to determine whether treating syphilis with azithromycin is as effective as the current recommended treatment, penicillin G. benzathine. Azithromycin offers many advantages over penicillin G. benzathine. Azithromycin is taken orally; penicillin G. benzathine is administered by injections that often are very painful and discourage patients from seeking treatment. In addition, the penicillin injections require refrigeration and needles, which can hamper administration in "field" settings. The azithromycin regimen proposed in this study could be administered as direct observed therapy in the field, using strategies modeled after those used to treat TB.

NIAID also has an active program in developing topical microbicides that may be especially important for protecting the health of women and children. With current global estimates exceeding 40 million people infected with HIV and the majority of these infections acquired through sexual intercourse, there is an increased need for the development of safe, effective, topically applied chemical and/or biologic barriers to prevent sexually transmitted HIV infection. Topical microbicides also may help prevent many other STIs. A topical microbicide is a preparation (e.g., gel, cream, 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 often must do with condoms. The ideal microbicide would be safe and nonirritating to the mucosal tissues, even if used on multiple occasions in a short period of time. In addition, microbicides should be inexpensive, unobtrusive, both fast and long acting, easy to store, and appealing to potential users. Topical microbicides should

be available in both spermicidal and nonspermicidal 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's research to develop topical microbicides to kill STI pathogens, including HIV, includes basic research, preclinical product development, and clinical evaluation. The Institute supports six Topical Microbicide Program projects and recently initiated the Microbicide Preclinical Development Program. NIAID, in conjunction with HPTN, is conducting clinical trials of topical microbicides at sites in the United States and in Pune, India, and is in the planning stages of other clinical and preclinical studies of topical microbicides. In addition, the Institute supports a topical microbicide candidate compound screening contract and is supporting grants funded under two topical microbicide initiatives from 2001 and 2002.

In all clinical research, including biomedical and behavioral studies, NIAID complies with the 1993 NIH *Guidelines on the Inclusion of Women and Minorities as Subjects in Clinical Research.* Congress mandated the establishment of these guidelines in the NIH Revitalization Act of 1993, and NIAID staff members participated in their development. The guidelines stipulate that women and members of minority groups must be included in all NIH-supported research projects involving human subjects, unless there is a compelling reason that such inclusion would be inappropriate. The guidelines also state that women of childbearing potential should not be routinely excluded from participation in clinical research.

In addition to funding research, NIAID supports conferences, meetings, and workshops. The Institute communicates research results to scientists through workshops and conferences and conveys medical information to the general public and physicians through its Office of Communications and Public Liaison. Every year, approximately 12,000 people call NIAID for information, and thousands more write for copies of pamphlets and other materials.