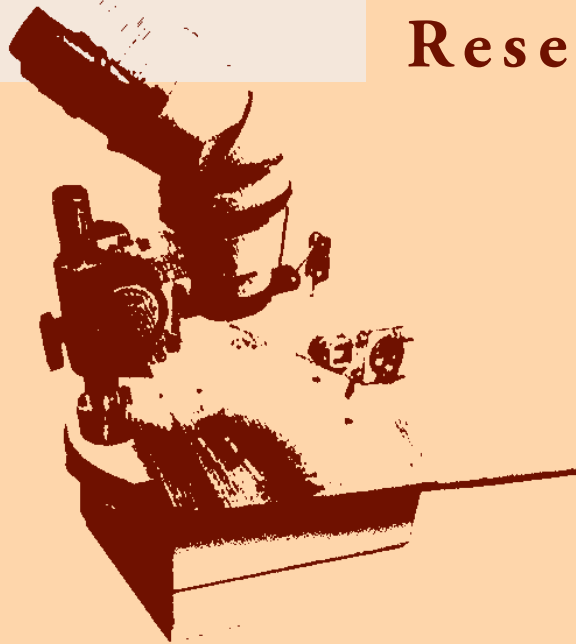




A Partnership for Health:



Minorities & Biomedical Research



National Institute of Allergy and Infectious Diseases

National Institutes of Health

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

2003–2004

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Executive Summary

The National Institute of Allergy and Infectious Diseases (NIAID) has long recognized that minority populations bear a disproportionate burden of sickness and disease in the United States.

Differences in racial and ethnic backgrounds can affect susceptibility to infectious and immunologic diseases, including acquired immunodeficiency syndrome (AIDS), asthma, sexually transmitted infections, and kidney disease. Moreover, minority populations often do not fully benefit from research advances that have helped improve the health of other Americans.

For more than 50 years, NIAID has progressed in understanding, treating, and preventing infectious and immunologic diseases known to occur disparately in minority populations. As outlined in its *Strategic Plan for Addressing Health Disparities*, NIAID continues to prioritize basic, clinical, and epidemiological research in addressing the health disparities in minority populations. Specifically, NIAID supports efforts to increase the participation of minority scientists in its research, increase the participation of the minority community in clinical research, and design targeted outreach activities for minority communities that communicate research developments and health risk.

Asthma and Allergic Diseases

Asthma morbidity and mortality have been increasing in the United States for the past 15 years and are particularly high among poor, African American, inner-city residents. For more than a decade, improving the management of asthma in children has remained a high priority for NIAID. Preliminary results from the Inner-City Asthma Study (1996–2001), co-sponsored by the National Institute of Environmental Health Sciences, indicate that physician education and an extensive environmental intervention can successfully reduce asthma symptoms among inner-city children and can continue to reduce symptoms 1 year after intervention. The Inner-City Asthma Consortium

(ICAC), established by NIAID in 2002, was created to evaluate the safety and effectiveness of promising immune-based asthma treatments developed to reduce asthma severity and prevent disease onset in inner-city children. ICAC will conduct research to determine the mechanisms of action of immune-based therapies; develop and validate biomarkers to measure disease stage, progression, and therapeutic effect; and understand the immunopathogenesis of asthma in inner-city children.

NIAID's Asthma and Allergic Diseases Research Centers program is the cornerstone of the pathobiology component of NIAID asthma and allergy research. This national network of centers conducts basic and clinical research on the mechanisms, diagnosis, treatment, and prevention of asthma and allergic diseases. In 2003, NIAID funded 4 Asthma and Allergic Diseases Research Centers, bringing the total number of centers to 13.

In 2003, NIAID requested applications for research projects aimed at understanding the early life changes in immune function that led to the development of asthma (RFA-AI-03-041 "Immune System Development and the Genesis of Asthma"). The Immune System Development and the Genesis of Asthma program will be launched in 2004 and will be co-funded by the National Heart, Lung, and Blood Institute (NHLBI). In response to provisions in the Children's Health Act of 2000 (P.L. 106-310), NIAID participates in the Federal Liaison Group for Asthma, a subcommittee of the National Asthma Education and Prevention Program.

Autoimmune Diseases

Collectively, autoimmune diseases afflict more than 5 percent of the U.S. population, and women are more likely to suffer from an autoimmune disease than men. Several autoimmune diseases, such as systemic lupus erythematosus (SLE) and scleroderma, disproportionately affect minority populations. NIAID supports a broad portfolio of

basic, preclinical, and clinical research aimed at understanding the pathogenesis of autoimmune diseases. Research programs include the Autoimmunity Centers of Excellence (ACE), the Autoimmune Disease Prevention Centers, and multidisciplinary research targeting the identification, characterization, and definition of gender-based differences in the immune response. In 2003, ACE was renewed and expanded to include nine separate institutions. Trials for new immunomodulatory interventions and studies of mechanisms of action are being developed. Centers are co-sponsored by the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) and the NIH Office of Research on Women's Health (ORWH). In fiscal year (FY) 2003, Autoimmune Disease Prevention Centers supported 14 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. The prevention centers are co-sponsored by NIDDK, the National Institute of Child Health and Human Development, ORWH, and the Juvenile Diabetes Research Foundation International (JDRE).

NIAID continues to support the Immune Tolerance Network (ITN). Co-sponsored by the NIDDK and JDRE, ITN is an international consortium of more than 80 investigators throughout the United States, Canada, and Europe dedicated to the clinical evaluation of novel, tolerance-inducing therapies for autoimmune diseases, asthma and allergic diseases, as well as the development of tolerance-inducing therapies to prevent the rejection of transplanted organs, tissues, and cells. NIAID supports the Multiple Autoimmune Disease Genetics Consortium (MADGC), a repository of genetic and clinical data and materials from families in which two or more individuals are affected by two or more distinct autoimmune diseases. MADGC has enrolled more than 150 families since May 2000. Established in FY 1998, NIAID continues to chair the Autoimmune Diseases Coordinating Committee (ADCC). The ADCC Autoimmune Diseases Research Plan was presented to Congress in 2002.

Transplantation

Organ transplantation represents a health disparity for African Americans and other minorities, who receive fewer transplants than would be expected from their representation on the transplant waiting list. NIAID supports a broad portfolio of research to address immune-mediated graft rejection, including basic research in transplantation immunology, preclinical evaluation of new therapies, and clinical trials of promising therapeutic approaches to improve short- and long-term graft survival. In 2003, NIAID renewed the Cooperative Clinical Trial in Pediatric Transplantation (CCTPT) program. CCTPT supports multicenter clinical trials of novel approaches to prevent acute and chronic graft rejection in pediatric kidney transplantation, evaluates modifications of immunosuppressive drug regimens to mitigate unwanted side effects of immunosuppression, and assesses pretransplant immunotherapy to improve transplantation outcomes. NIAID's Division of Allergy, Immunology and Transplantation and NIAID's Division of AIDS launched a study on the outcomes of kidney and liver transplantation for HIV-positive (HIV+) patients in 2003. The primary aim of this prospective, multicenter cohort study is to evaluate the safety and efficacy of solid organ transplantation in HIV+ patients who undergo kidney or liver transplantation.

In 2001, NIAID and NHLBI renewed the Immunopathogenesis of Chronic Graft Rejection Program, designed to enhance knowledge of chronic graft failure. NIAID, in collaboration with NIDDK, supports the Non-Human Primate Immune Tolerance Cooperative Study Group to evaluate the safety and efficacy of novel tolerogenic regimens in preclinical animal models of kidney and islet transplantation. The study group was renewed in 2002, adding several new research centers.

NIAID, along with several NIH Institutes and Centers, and JDRE, continues to support the International Histocompatibility Working Group

(IHWG). IHWG, a network of more than 200 laboratories in 44 countries, collects and shares data on the human leukocyte antigen (HLA) gene complex.

Recently, IHWG investigators joined forces with Hematopoietic Stem Cell Transplant Centers to develop an international database of transplantation outcomes and donor-recipient HLA genotypes. NIAID, with the National Center for Minority Health and Health Disparities, continues to support the demonstration and education research projects aimed at increasing minority involvement in organ donor registries. The Louisiana Legacy Donor Registry is working to increase organ donations by using new and nontraditional approaches to donor recruitment, improving the consent process, and facilitating the medical community's access to donor registry information. NIAID continues to support the Minority Community Outreach Program on Organ Donation and Transplantation at the Hope Heart Institute in Seattle, Washington. A second research project at the Hope Heart Institute seeks to increase organ donation among rural American Indians and Alaska Natives.

Tuberculosis

During 2000, approximately 78 percent of active tuberculosis (TB) cases were reported among racial and ethnic minorities. Problems of urban poverty, high HIV infection rates, and the effects of household overcrowding may contribute to the disproportionate impact of TB on minorities.

Over the past decade, NIAID has dramatically boosted funding for TB research, which has allowed the Institute to support a number of initiatives and a markedly expanded community of TB researchers. NIAID's extramural TB research program currently supports more than 231 grants for basic, applied, and clinical research, including awards to support the genomic sequencing of *Mycobacterium tuberculosis* (*M.tb*) and other strains of the bacterium that cause TB.

NIAID continues to support the Tuberculosis Research Unit at Case Western Reserve University,

established to conduct clinical trials of potentially new TB therapeutic, preventive, and diagnostic strategies. NIAID's *Blueprint for TB Vaccine Development*, presented at the 1998 International Symposium for Tuberculosis Vaccine Development and Evaluation, outlines the specific steps needed to develop improved TB vaccines. A task force will oversee the implementation of the blueprint. NIAID's Vaccine Treatment and Evaluation Unit in St. Louis, Missouri, will work with the Global Vaccine Foundation to conduct a phase I safety and immunogenicity trial on a new anti-TB vaccine (recombinant bacille Calmette-Guerin vaccine), expected to begin in early spring 2004.

Through the Tuberculosis Research Materials and Vaccine Testing contract at Colorado State University, NIAID provides TB research reagents to qualified investigators throughout the world. During 2003, 121 individual vaccines or adjuvant candidates have been tested, with 15 vaccine testing experiments completed, 16 experiments in process, and 7 under development. The Southern Research Institute in Birmingham, Alabama, maintains an NIAID-supported Tuberculosis Antimicrobial Acquisition and Coordinating Facility (TAACF). TAACF has contacted more than 3,500 chemists throughout the world seeking candidate anti-TB compounds. More than 60,000 candidate anti-TB compounds have been received from academic and private-sector investigators, principally in the United States and Europe, with growing involvement of scientists from Africa, Asia, Australia, South America, and other geographic sites.

Sexually Transmitted Infections

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. Reported rates of some STIs, such as gonorrhea and syphilis, are as much as 30 times higher for African Americans than for whites. This disparity is due to many factors, including differences in the distribution of poverty, health-seeking behaviors, and access to quality health care. NIAID supports individual investigator-initiated research grants and

a variety of research programs for the development of more effective prevention and treatment approaches for STIs. Research efforts include developing and licensing vaccines, topical microbicides, and treatments for microbes that cause STIs; understanding the long-term health impact of sexually transmitted pathogens in various populations; stimulating basic research on the pathogenesis, immunity, and structural biology of these pathogens; and developing better and faster diagnostics.

NIAID's ongoing efforts include the STD Cooperative Research Centers, the STD Clinical Trials Unit, and the Topical Microbicides Program Projects. NIAID recently intensified efforts in syphilis research, especially in the development of new, improved biomedical tools to complement and sustain CDC's Syphilis Elimination Program. In addition, NIAID continues to initiate and support a variety of other STI research projects, including the development and evaluation of STI diagnostics designed for point-of-care use through the Small Business Innovation Research mechanism, grants for the development of vaccines to prevent chlamydial and gonorrheal infections, and a herpes vaccine efficacy trial.

Hepatitis C

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. At the same time, available HCV treatments are less effective for African Americans than other populations.

NIAID has aggressively pursued the expansion of HCV research through its development of the "Hepatitis C Framework for Progress." With the aid of participating Institutes and Centers, an NIH-wide framework was drafted that incorporates varying individual missions into a cohesive global plan. NIAID is investigating clinical manifestations to develop noninvasive methods to evaluate current disease state, to predict outcomes, and to prevent or reverse disease progression.

Currently, NIAID provides funding support to six hepatitis C Cooperative Research Centers, one of the cornerstones of NIAID's HCV research. Other NIAID HCV research activities include partial support for the ancillary studies of the NIDDK-sponsored trial "Hepatitis C Antiviral Long-term Treatment against Cirrhosis (HALT-C)"; the development of robust and economical cell culture and animal models; support for two antiviral screening tools via its *in vitro* screening contract programs; activities to broaden HCV research and development; the "Liver and Pancreatic Disease in HIV Infection" program announcement sponsored jointly with NIDDK to stimulate research on the pathogenesis and therapeutics of liver and pancreatic disease associated with the co-infections (e.g., hepatitis B, hepatitis C) that occur in patients with HIV infection; and research investigating the relationships between hepatitis C virus replication, evolution, and disease progression in American Indians and Alaska Natives.

Pneumonia

Pneumococcal pneumonia is an infection in the lungs caused by the *Streptococcus pneumoniae*. Rates of invasive infection increase with age and are disproportionately higher among certain minority populations. NIAID supports an efficacy and safety phase III randomized trial in 8,292 Navajo and White Mountain Apache children using the licensed 7-valent pneumococcal conjugate vaccine, Prevnar. This study shows that Prevnar is capable of preventing disease in the general U.S. population.

Acquired Immunodeficiency Syndrome

Although AIDS affects all racial groups, the disease continues to disproportionately affect minority populations. African Americans and Hispanics constitute 61 percent of the AIDS cases in the United States. Of the new AIDS cases reported in 2002, 55 percent were African American, 13 percent Hispanic, 32 percent white, and less than 1 percent American Indian, Alaska Native, and Asian-Pacific Islander. Among women, African Americans and Hispanics account for 81 percent of AIDS cases. Among men, African Americans and

Hispanics account for 64 percent of cases. Minority children also are disproportionately affected by AIDS.

As the HIV/AIDS epidemic continues to expand in minority communities, enrolling minority patients in HIV/AIDS clinical trials is particularly urgent. People of minority backgrounds face unique social, economic, and medical issues when coping with the challenges associated with HIV/AIDS infection, and, therefore, one of the greatest challenges facing HIV/AIDS researchers today is the recruitment and retention of minority patients for clinical trials. An additional challenge is the recruitment of underrepresented minority investigators to AIDS and AIDS-related clinical and basic research disciplines. Consequently, 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 directs a large therapeutic clinical trials program consisting of three groups: the Adult AIDS Clinical Trials Group (AACTG), the Pediatric AIDS Clinical Trials Group (PACTG), and the Terry Beinr Community Programs for Clinical Research on AIDS (CPCRA). AACTG, PACTG, and CPCRA strive to ensure that a sufficient proportion of minority individuals is enrolled in clinical trials.

NIAID's HIV/AIDS clinical research networks provide opportunities for community representatives to participate in the research process through local, national, and international Community Advisory Boards. In addition, NIAID recently released the "Enrolling Women and Minorities in HIV/AIDS Research Trials" program announcement to fund innovative approaches to access, enroll, and retain women and racial/ethnic minorities in HIV/AIDS research trials in the United States.

NIAID's epidemiologic research explores the clinical course and factors contributing to the transmission of HIV/AIDS infection in a variety of populations. NIAID supports several studies including the

Women and Infants Transmission Study, which targets inner-city women and their children; the Women's Interagency HIV/AIDS Study, which explores the clinical course of HIV/AIDS infection in women with a focus on minority women; and the Multicenter AIDS Cohort Study, a prospective, longitudinal study of HIV/AIDS disease in homosexual and bisexual men.

NIAID continues to support efforts to develop an effective HIV vaccine. Established in 2000, the HIV Vaccine Trials Network (HVTN) is a collaboration of domestic and international clinical sites dedicated to developing a preventive HIV vaccine. HVTN tests and evaluates candidate vaccines in clinical trials. There are 18 sites in the United States and 13 sites overseas, including sites in Africa, Asia, South America, and the Caribbean. HVTN's global capacity will allow for rapid expansion and the ability to perform large-scale studies of suitable vaccines as more vaccine candidates enter the pipeline for testing and development. Currently, HVTN is conducting six phase I and two phase II clinical trials of candidate HIV vaccines. In addition to conducting clinical studies, HVTN develops community outreach programs to educate people about HIV/AIDS and vaccine research.

NIAID is currently in the second year of its HIV Vaccine Communications Campaign. Targeting at-risk populations, the HIV Vaccine Communications Campaign is developing and implementing a national education campaign to increase awareness and support for HIV vaccine research, especially in at-risk populations. This past year, a national survey was completed that evaluated the attitudes toward and knowledge of HIV vaccine research in the general population, as well as in segmented groups of African Americans, Hispanics, and men who have sex with men. The Communications Campaign is working to correct the misperceptions that exist regarding HIV vaccine trials and, at the same time, provide general information about HIV vaccine research to minority communities.

NIAID established the HIV Prevention Trials Network (HPTN) in 2000 in an effort to reduce the worldwide spread of HIV. HPTN is a global network of clinical trial sites with 9 sites in the United States and 16 international sites in Africa, Asia, Europe, and South America. The network explores a variety of nonvaccine prevention strategies to reduce HIV/AIDS transmission, such as testing and developing biomedical and behavioral intervention programs. Additional prevention efforts include research to prevent mother-to-child transmission of HIV; evaluation of simpler and less costly prevention regimens suitable for global use; support for the Centers for AIDS Research, which address problems in the enrollment and retention of women and minority groups in AIDS clinical trials; and promotion of the development of minority scientists in AIDS research.

NIAID Outreach Activities

Disseminating research results to the media, health professionals, and the public is an important aspect of NIAID's mission. Outreach activities include producing and publicizing print, audiovisual, and Web-based materials; distributing materials at professional and community meetings; and sponsoring workshops and conferences for community health care providers and the public. Materials such as press releases, information sheets, and booklets are distributed worldwide in response to more than 10,000 requests from people who contact NIAID each year. The NIAID Web site is visited 1.5 million times each month. Hundreds of thousands of inquirers request materials or download information from the NIAID Web site each year. Periodic e-mails provide NIAID research news and information on advances that specifically relate to an organization's research interests.

Minority Researchers' Training and Enhancement Programs

Through innovative programs and outreach efforts, NIH continually works to increase the number of minority researchers in the field of biomedical research. In addition to supporting NIH-wide programs, NIAID supports a variety of minority

programs for biomedical research, from high school through postdoctoral training. NIAID's Office of Special Populations and Research Training (OSPRT) is engaged in an extensive outreach campaign targeting colleges, universities, medical centers, and professional organizations to encourage the participation of minority investigators in NIAID research activities. OSPRT programs include the Introduction to Biomedical Research Program (IBRP) and the Bridging the Career Gap for Underrepresented Minority Scientists workshop. In addition, OSPRT plays a key role in reporting data about women and minority inclusion in phase III clinical trials and serves as NIAID's coordinator and liaison for the Institute's *Strategic Plan for Addressing Health Disparities*.

IBRP seeks to encourage academically talented members of minority groups to pursue careers in life sciences and biomedical research through its extramural and intramural research arms. The Richard M. Asofsky Scholars In Research (ASIR) is the IBRP extramural arm and is administered through OSPRT. The intramural arm of IBRP is known as the Introduction to NIAID Research Opportunities (INRO) and is administered through the Division of Intramural Research's Office of Special Emphasis.

The ASIR program provides opportunities for underrepresented minority students to work with extramural principal investigators in a mentorship relationship.

In FY 2003, INRO provided qualified minority students with a 3-day program that introduced them to research opportunities at NIAID and included scientific lectures and tours of some of the NIAID laboratories.

NIAID also collaborates with minority organizations to disseminate information about biomedical research careers to members of underrepresented groups. The Research Centers in Minority Institutions (RCMI) program provides grant support to predominantly minority health professional schools and graduate institutions that offer a doctorate in the health professions or health-

related sciences for the purpose of strengthening and augmenting their human and physical resources for conducting biomedical or behavioral research. Currently, 17 institutions participate in the RCMI program.

The Interamerican College of Physicians and Scientists (ICPS) is one outreach activity supported by OSPRT that targets a specific underrepresented community. Founded in 1979, ICPS promotes cooperation among U.S. Hispanic physicians and seeks to advance their professional and educational development. ICPS is the only national organization representing Hispanic physicians.

Targeting individuals who receive NIAID minority training and research supplemental awards, the Bridging the Career Gap program seeks to provide young, minority investigators with the tools and information needed for a successful career in biomedical research. The initiative consists of a 2-day seminar addressing career choices, networking, the importance of selecting the right mentor, and the NIH grant system and components.

NIAID continues to work with schools on several programs that foster an interest in science and research careers among younger students. The Institute supports the Partners in Education Program that provides students in the Washington, DC, area with a scientific environment in which they can nurture their interest in the sciences. In FY 2001, NIAID co-funded the Temple University Minority Access to Biomedical Research Careers partnership program. The goal of the program is to provide additional math and science instruction to outstanding minority middle school students and encourage them to pursue graduate degrees in biomedical research. NIAID's Rocky Mountain Laboratories teamed with local middle and high schools in Montana to present a program that introduces students to biomedical research.

NIAID continues to strengthen its research on infectious and immunologic diseases that contribute to health disparities experienced by minority populations, as well as programs designed to build a new cadre of minority researchers. These efforts, coupled with the Institute's increased outreach to minority groups, will help ensure that NIAID research benefits all individuals in the United States.

I. Minority Health Initiatives

Allergy, Immunology and Transplantation

NIAID's *Strategic Plan for Addressing Health Disparities* outlines two main objectives with respect to minority health in the areas of allergy, immunology, and transplantation:

- Support basic and clinical research on immune-mediated diseases, including asthma and allergic diseases, autoimmune diseases, and rejection of transplanted organs, tissues, and cells, that will lead to a better understanding of these diseases and improved prevention and treatment strategies.
- Increase the number of minority biomedical scientists through individual and institutional support for undergraduate, graduate, and postgraduate research training in a variety of disciplines related to immune-mediated diseases.

Asthma and Allergic Diseases

Asthma and allergic diseases are among the major causes of illness and disability in the United States. Approximately 50 percent of Americans have positive skin tests to at least 1 of 10 allergens that contribute to allergic illness (NHANES III, the 1987–1994 National Health and Nutrition Examination Survey. *J Allergy Clin Immunol* 2002;110:381-7). Chronic allergic conditions can significantly decrease personal quality of life, patient well-being, employee productivity, and school performance and attendance. Compared with white children of the same age, African American children have a higher prevalence of allergy to cockroaches, house dust mites, and molds (*Alternaria*). Similarly, Mexican American children have a higher prevalence of allergy to cockroaches and house dust mites (NHANES III. *J Allergy Clin Immunol* 2001;108:747-52).

Asthma affects more than 17 million Americans, resulting in more than 500,000 hospitalizations and 5,000 deaths annually. African Americans are disproportionately affected by asthma. In 2001, the

current asthma prevalence among non-Hispanic African Americans was approximately 10 percent higher than among non-Hispanic whites and approximately 40 percent higher than among Hispanics. Non-Hispanic African Americans had an asthma attack prevalence about 20 percent higher than among non-Hispanic whites and almost 60 percent higher than among Hispanics (Centers for Disease Control and Prevention [CDC], "Asthma Prevalence, Health Care Use and Mortality, 2000-2001," National Center for Health Statistics, January 28, 2003. www.cdc.gov/nchs/products/pubs/pubd/hestats/asthma/asthma.htm). The disparity in asthma prevalence was also greater among African American children: asthma was more prevalent among African American children younger than 18 years (7.4 percent) than among white children (5.0 percent) of the same age (*Pediatrics* 2002;110:317). In 1998, asthma accounted for an estimated \$12.7 billion in expenditures, with \$7.4 billion in direct medical expenditures and \$5.3 billion in indirect costs (*J Allergy Clin Immunol* 2001;107:3-8).

Asthma is a long-term, generally progressive lung disease characterized by episodes of obstructed airways. The cellular infiltrates and inflammatory mediators of asthma are thought to be similar to those of other allergic diseases, but asthma mediators also appear to cause airway hyperreactivity. Chronic inflammation of the airways is recognized widely as a key factor in the development of asthma, and, as a result, anti-inflammatory medications have become a mainstay of asthma therapy. Many immune-based therapies are in the early stages of development or are being studied as investigational agents. However, much needs to be learned before the more promising immune-based approaches can be developed into licensed therapies.

Although allergic reactions are an important cause of asthma, nonimmunologic factors (e.g., viral infections, exposure to environmental tobacco smoke and pollutants) also contribute to the pathophysiology of this disease. Recent studies

suggest that the development of asthma begins around the first months of gestation. These and other promising findings offer new opportunities to initiate basic and clinical research aimed at clearly defining the early-life perturbations of the immune system that lead to the development of asthma.

For more than a decade, improving the management of asthma in children has remained a high priority for NIAID. Preliminary results from the Inner-City Asthma Study (1996-2001), co-sponsored by the National Institute of Environmental Health Sciences, indicate that physician education and an extensive environmental intervention can successfully reduce asthma symptoms among inner-city children and can continue to reduce symptoms 1 year after intervention. The environmental intervention involved home-based education to reduce exposure to environmental triggers, including environmental tobacco smoke, cockroaches, house dust mites, mold, furry pets, and rodents. Data show that the environmental intervention resulted in 2 to 4 weeks of additional symptom-free days, a reduction in unscheduled medical visits, and improvements in asthma symptoms. The physician feedback intervention provided physicians with up-to-date information on patients' asthma symptoms, medication, and health care utilization. Data show that the physician feedback intervention resulted in a 20 percent decrease in unscheduled visits for poorly controlled asthma. The final results of the Inner-City Asthma Study should reveal significantly improved health for inner-city children with asthma, as well as an overall reduction of the high medical, economic, and social costs associated with this disease. The Inner-City Asthma Consortium (ICAC), established by NIAID in 2002, will evaluate the safety and efficacy of promising immune-based asthma treatments developed to reduce asthma severity and prevent disease onset in inner-city children. ICAC will conduct research to determine the mechanisms of action of immune-based therapies; develop and validate biomarkers to measure disease stage, progression, and therapeutic effect; and conduct research to understand the immunopathogenesis of asthma in inner-city children.

NIAID's Asthma and Allergic Diseases Research Centers program is the cornerstone of the pathobiology component of NIAID asthma and allergy research. This national network of centers conducts basic and clinical research on the mechanisms, diagnosis, treatment, and prevention of asthma and allergic diseases. In 2003, NIAID funded 4 new Asthma and Allergic Diseases Research Centers, bringing the total number of centers to 13.

In 2003, NIAID requested applications for research projects aimed at understanding the early life changes in immune function that lead to the development of asthma (RFA-AI-03-041 "Immune System Development and the Genesis of Asthma"). Identifying the cellular and molecular processes involved in the onset of asthma provides the basis for devising novel and effective immune-based strategies for the treatment and prevention of this disease. This approach will allow researchers to develop strategies that do not compromise immune system integrity and are not hampered by the limitations inherent in current therapies. The Immune System Development and the Genesis of Asthma program will be launched in 2004 and will be co-funded by the National Heart, Lung, and Blood Institute (NHLBI).

In response to provisions in the Children's Health Act of 2000 (P.L. 106-310), NIAID participates in the Federal Liaison Group for Asthma, a subcommittee of the National Asthma Education and Prevention Program.

Autoimmune Diseases

Autoimmune diseases are caused by the misdirection of an immune response toward the body's own tissues, causing the immune system mistakenly to attack the body's own cells, tissues, and organs. People suffering from autoimmune diseases often endure loss of function, disability, hospitalizations, outpatient visits, decreased productivity, and impaired quality of life. Autoimmune diseases include systemic lupus erythematosus (SLE), type 1 diabetes, scleroderma, multiple sclerosis, Crohn's disease, Graves disease, and rheumatoid arthritis. Collectively, autoimmune

diseases afflict more than 5 percent of the U.S. population, and women are more likely to suffer from an autoimmune disease than men. Several autoimmune diseases, such as systemic lupus erythematosus and scleroderma, disproportionately affect minority populations.

SLE, or “lupus,” is a chronic, inflammatory, multisystem disorder of the immune system in which the body produces antibodies that target the body’s healthy cells and tissues. SLE occurs in 1 of 2,000 Americans with varying severity. SLE is more common and more severe in African American women, occurring in as many as 1 in 250 young African American women. SLE is twice as prevalent among African American men as among white men. Reports also indicate an increased prevalence of SLE and rheumatoid arthritis among many American Indian and Alaska Native tribes.

Scleroderma is an autoimmune disease involving the abnormal growth of connective tissues supporting the skin and internal organs. There are two main classes of scleroderma: localized and systemic. Localized scleroderma affects the skin and musculoskeletal system. Systemic scleroderma affects the skin and musculoskeletal system and can also affect blood vessels and damage the heart, lungs, and kidneys. The number of Americans affected by systemic scleroderma is estimated to range from 40,000 to 165,000. Systemic scleroderma affects more African American women than women of European descent.

NIAID supports a broad portfolio of basic, preclinical, and clinical research aimed at understanding the pathogenesis of autoimmune diseases. Researchers investigate new ways to modify the immune system and will apply this knowledge to the identification and evaluation of promising approaches to treat and prevent autoimmune diseases. Research programs include Autoimmunity Centers of Excellence (ACEs); Autoimmune Disease Prevention Centers; and multidisciplinary research targeting the identification, characterization, and definition of gender-based differences in the immune response.

The ACEs support collaborative basic and clinical research on autoimmune diseases, including pilot clinical trials of immunomodulatory therapies. In 2003, the ACEs were renewed and expanded to include nine separate institutions. The centers bring together subspecialists (e.g., neurologists, gastroenterologists, rheumatologists) and basic scientists to increase clinical and research collaborations on autoimmunity. These centers conduct clinical trials to evaluate therapeutic interventions for several autoimmune diseases, including SLE. Trials for new immunomodulatory interventions and studies of mechanisms of action are being developed. The ACEs are co-sponsored by the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) and the NIH Office of Research on Women’s Health (ORWH).

The Autoimmune Disease Prevention Centers conduct basic research on the development of new targets and approaches to prevent autoimmune diseases. In fiscal year (FY) 2003, Autoimmune Disease Prevention Centers supported 14 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. The centers continue to evaluate supported projects through pilot and clinical studies. The prevention centers are co-sponsored by NIDDK, the National Institute of Child Health and Human Development (NICHD), ORWH, and the Juvenile Diabetes Research Foundation International (JDRF).

NIAID established the “Sex-Based Differences in the Immune Response” (RFA-AI-01-005) research initiative in 2001 to better understand differences in immune response between males and females. Research supported under this initiative will identify, characterize, and define sex- and gender-based differences in immune responses. Studies include basic and clinical investigations of sex differences regulated by hormonal and nonhormonal mechanisms in response to exogenous antigens, the innate and adaptive immune response, and systemic and mucosal immunity. This initiative is co-sponsored by the National Institute of Neurological Disorders and Stroke, the National

Institute of Arthritis and Musculoskeletal and Skin Diseases, ORWH, and the National Multiple Sclerosis Society.

NIAID continues to support the Immune Tolerance Network (ITN). Co-sponsored by NIDDK and JDRE, ITN is an international consortium of more than 80 investigators throughout the United States, Canada, and Europe. Investigators are dedicated to the clinical evaluation of novel, tolerance-inducing therapies for autoimmune diseases, asthma and allergic diseases; and the development of tolerance-inducing therapies to prevent the rejection of transplanted organs, tissues, and cells. The goal of tolerance-inducing therapies is to “re-educate” the immune system to eliminate injurious immune responses and graft rejection, while preserving protective immunity against infectious agents. ITN conducts integrated studies on the underlying mechanisms of approaches and develops and evaluates markers and assays to measure the induction, maintenance, and loss of tolerance in humans. More information about ITN is available at www.immunetolerance.org.

The NIAID Clinical Trials Network for Stem Cell Transplantation for Autoimmune Diseases will evaluate the safety and efficacy of hematopoietic stem cell transplantation for treating severe autoimmune diseases, including SLE and scleroderma.

NIAID supports the Multiple Autoimmune Disease Genetics Consortium (MADGC), a repository of genetic and clinical data and materials from families in which two or more individuals are affected by two or more distinct autoimmune diseases. MADGC provides materials to advance research aimed at discovering the human immune response genes involved in autoimmunity. MADGC has enrolled more than 150 families since May 2000. More information can be found at www.madgc.org.

NIAID chairs the NIH Autoimmune Diseases Coordinating Committee (ADCC), established in FY 1998 at the request of Congress to increase collaboration and facilitate coordination of research

among NIH Institutes and Centers, other Federal agencies, and private groups interested in these diseases. The ADCC Autoimmune Diseases Research Plan was presented to Congress in 2002. The research plan can be found at www.niaid.nih.gov/dait/pdf/ADCC_Report.pdf.

Transplantation

The principal goal of transplantation is the physical and functional replacement of failing organs and tissues. The most striking advances in transplantation have come in the past 30 years, with improvements in surgical techniques and the development of immunosuppressive agents to inhibit a recipient’s immune responses against grafts. These advances have made transplantation the preferred treatment for many end-stage organ diseases. Today, transplantation procedures are performed using more than 25 different organs and tissues with first-year graft survival rates often exceeding 80 percent. Despite these successes, two major impediments remain: immune-mediated graft rejection and the critical shortage of donor organs. The primary reason for graft failure is a recipient’s vigorous immune response to the graft. Improvements in immunosuppressive therapy have dramatically increased graft survival for all organs during the first year after transplantation. However, long-term graft survival has not improved significantly in the past two decades because of chronic graft failure. The mechanisms of chronic graft failure differ from those of acute rejection and are less well understood.

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

Immune-Mediated Graft Rejection

Although advances in surgical procedures and immunosuppressive therapies have greatly increased, 1-year graft survival rates for all organs and tissues and long-term graft survival is relatively unchanged. NIAID supports a broad portfolio of research to address immune-mediated graft rejection, including basic research in transplantation immunology, preclinical evaluation of new therapies, and clinical trials of promising therapeutic approaches to improve short- and long-term graft survival. The major goals of transplantation research are to understand the pathways whereby the immune system recognizes transplanted organs, tissues, and cells; characterize the cellular and molecular components of acute rejection and chronic graft failure; evaluate novel therapies for treating rejection and prolonging graft survival in preclinical models; develop and implement strategies for immune tolerance induction; and conduct clinical trials of new therapies to improve graft survival while minimizing the toxic side effects of immunosuppressive drugs.

Kidney transplantation accounts for 59 percent of all solid-organ transplant procedures and is the preferred therapy for end-stage renal disease (Organ Procurement and Transplantation Network. www.optn.org). In 2003, NIAID renewed the Cooperative Clinical Trials in Pediatric Transplantation (CCTPT) program. The program supports multicenter clinical trials of novel approaches to prevent acute and chronic graft rejection in pediatric kidney transplantation, evaluates modifications of immunosuppressive drug regimens to mitigate unwanted side effects of immunosuppression, and assesses pretransplant immunotherapy to improve transplantation outcomes. Clinical trials that continue to accrue subjects include a study comparing the immunosuppressive drug sirolimus to the standard treatment for chronic graft failure, a study of the effects of steroid withdrawal in pediatric transplant recipients, an evaluation of intravenous immunoglobulin as an agent to reduce existing immunity to potential donor organs, and the study of transplantation for high-risk kidney transplant candidates. CCTPT conducts mechanistic studies

to determine the effect of these interventional approaches on the immune system. The mechanistic studies have led to novel approaches for noninvasive diagnosis of acute rejection as well as innovative approaches for detecting T cells that may regulate the immune response to grafts.

Patients infected with HIV/AIDS are at significant risk for end-stage organ disease. Before the advent of highly active antiretroviral therapy (HAART), HIV-positive (HIV⁺) patients often were not considered for transplants on the basis of poor prognosis. HAART has significantly increased the number of HIV⁺ patients with end-stage kidney or liver disease as potential candidates for transplantation. NIAID's Division of Allergy, Immunology and Transplantation and NIAID's Division of AIDS launched a study on the outcomes of kidney or liver transplantation for HIV⁺ patients in 2003. The primary aim of this prospective, multicenter cohort study is to evaluate the safety and efficacy of solid organ transplantation in HIV⁺ patients who undergo kidney or liver transplantation.

Despite substantial improvements in short-term graft survival, long-term graft survival remains poor, primarily because of chronic graft failure. In 2001, NIAID and NHLBI renewed the Immunopathogenesis of Chronic Graft Rejection Program, designed to enhance knowledge of chronic graft failure. Little is known about the etiology of chronic graft failure, including the factors that determine onset and severity, the targets of immune reactivity, and the factors that control the degree of variability in the rejection process between patients. The Immunopathogenesis of Chronic Graft Rejection Program will enhance understanding of both the immunologic and nonimmunologic mechanisms that underlie chronic graft failure rejection of solid organs, improve diagnostic criteria to predict graft failure, and identify novel approaches for clinical intervention.

Improvements in immunosuppressive therapy have dramatically reduced acute graft rejection and have increased the 1-year graft survival rate for all organ transplants. However, many serious side effects

such as infections and malignancies are associated with the use of systemic immunosuppressive drugs to prevent graft rejection. Reducing the risk of serious side effects while improving graft and patient survival is a priority in transplantation immunology. One promising alternative to immunosuppression is to interrupt or modify the immune response to establish specific tolerance to the graft. NIAID, in collaboration with NIDDK, supports the Non-Human Primate Immune Tolerance Cooperative Study Group. The goal of this program is to evaluate the safety and efficacy of novel tolerogenic regimens in animal models of kidney and islet transplantation. The study group has demonstrated long-term graft acceptance using tolerogenic regimens in both kidney and islet allograft recipients. The study group was renewed in 2002, adding several new research centers. The new research centers will allow a larger number of tolerance-induction strategies to be rigorously evaluated. NIAID supports breeding colonies of rhesus and cynomolgus macaques to accelerate the research conducted through this program.

Histocompatibility and Immunogenetics

NIAID, along with several NIH Institutes and Centers, and JDRF, continues to support the International Histocompatibility Working Group (IHWG). IHWG, a network of more than 200 laboratories in 44 countries, collects and shares data on the human leukocyte antigen (HLA) gene complex. Researchers seek to (1) advance histocompatibility testing by discovering new HLA alleles and developing new tissue-typing reagents and methods, (2) elucidate HLA associations with autoimmune diseases, and (3) improve the outcomes of hematopoietic stem cell (HSC) transplantation through better donor-recipient matching. Recently, IHWG investigators joined forces with HSC transplant centers to develop an international database of transplantation outcomes and donor-recipient HLA genotypes. The international database will help determine optimal matching criteria for HSC transplants between unrelated individuals and increase transplantation access for ethnically diverse populations. In

addition, IHWG researchers are working to identify single nucleotide polymorphisms (SNPs) in immune-response genes. SNPs may account for the increased susceptibility of certain individuals or groups to immune-mediated diseases. SNP data have been gathered for more than 100 immune-response-related genes. More information about the IHWG can be found at www.ihwg.org.

Donor Organ Shortage

In 2001, a total of 24,897 organ transplants were performed in the United States, including 14,774 kidneys, 5,328 livers, 2,154 hearts, 554 pancreata, 1,042 lungs, 107 intestines, 33 heart-lung combinations, and 905 kidney-pancreas combinations. For the second consecutive year, living donors exceeded deceased donors (6,617 versus 6,183) (Organ Procurement and Transplantation Network, September 5, 2003. www.optn.org). However, the limited availability of donor organs is the main factor that restricts the number of transplantation procedures performed each year in the United States. The waiting list for transplants has quadrupled in size since 1988 to more than 80,000 patients, and, as a result, 6,482 patients died in 2002 while awaiting transplants. NIAID supports efforts to increase organ donation by improving donor registries and developing and testing educational interventions. Efforts to increase organ donation emphasize the involvement of African Americans and other underrepresented minority populations that are at greater risk of end-stage renal disease.

NIAID, with the National Center for Minority Health and Health Disparities, continues to support demonstration and education research projects aimed at increasing minority involvement in organ donor registries. The Legacy Donor Registry in Louisiana is working to increase organ donation by using new and nontraditional approaches to organ donor recruitment, improving the consent process to enhance organ donations, and facilitating the medical community's access to donor registry information. The program's Corporate Donor Program began in 2000 and has conducted organ

donation awareness events that reach major Louisiana corporations and employers. More information about the Legacy Donor Registry can be found at www.lopa.org/about_leg_rg.php.

NIAID continues to support the Minority Community Outreach Program on Organ Donation and Transplantation at the Hope Heart Institute in Seattle, Washington. This unique community-based outreach network is dedicated to increasing organ donation among minority populations in Seattle and Tacoma, Washington. Projects supported by the program involve (1) the development and distribution of educational materials in African American and Asian communities, (2) public service announcements at Department of Motor Vehicles offices, and (3) the development of a computerized database of community residents to record donation preferences, educational levels, and medical histories. A second research project developed by the Hope Heart Institute includes an educational video, "New Traditions of Sharing: Alaska Native Stories of Organ Donation and Transplantation" and other culturally sensitive educational materials that seek to increase organ donation among rural Alaska Natives.

Microbiology and Infectious Diseases

The microbiology and infectious diseases segment of NIAID's scientific agenda includes intramural and extramural research to control and prevent diseases in humans caused by virtually every infectious agent except HIV. NIAID supports a wide spectrum of projects ranging from basic biomedical research (e.g., studies of microbial physiology and antigenic structure) to applied research (e.g., developing diagnostic tests and clinical trials to evaluate potential drugs and vaccines).

Tuberculosis

A century ago, tuberculosis (TB) was a leading cause of death in the United States. Through the efforts of physicians, researchers, public health

officials, improvements in living conditions, and the introduction of effective drug therapies, the number of TB cases and deaths in the United States declined steadily from the early 20th century until 1985.

Because of the HIV epidemic, new cases of TB in the United States increased unexpectedly between 1985 and 1992. Starting in 1992, however, a large influx of Federal funds and a renewed emphasis on TB therapy, prevention, and control have led to declining TB cases and death rates in the United States. During 2002, a total of 15,078 TB cases were reported to the CDC. This number represents a 5.7-percent decline in the number of reported TB cases from 2001, a 43.5-percent decline in reported TB cases from the 1992 peak of the TB resurgence, and the lowest recorded TB rate in the United States since reporting began in 1953 (CDC. *MMWR* March 21, 2003).

The continued downward trend in reported TB cases is thought to reflect at least six factors:

- Improved laboratory methods for prompt identification of *Mycobacterium tuberculosis* (*M.tb*)
- Broader use of drug susceptibility testing
- Expanded use of preventive therapy in high-risk groups
- Implementation of measures to limit transmission of *M.tb* in congregate settings (e.g., hospitals, homeless shelters, and HIV/AIDS treatment facilities)
- Improved follow-up of diagnosed cases
- Increased Federal resources

Despite progress in TB reduction over the past 10 years, TB remains a matter of grave concern. Overall, national declines in TB incidence mask substantial disparities between rates in the majority of U.S. residents and rates in two specific populations. Foreign-born minorities and U.S.-born non-Hispanic African Americans now

account for approximately three-fourths of the TB cases in the United States (CDC. *MMWR* March 21, 2003). A combination of factors is responsible for the disproportionate impact of TB on minorities. Foreign-born minorities emigrating from TB-endemic countries may harbor TB infection or already have active TB disease when they move to the United States. In addition, urban poverty, high HIV infection rates, and the effects of household overcrowding may contribute to the disproportionately high number of TB cases in minority populations.

The link between HIV/AIDS and TB is thought to be a significant factor in the spread of TB. Worldwide, TB is the leading cause of death in individuals with HIV/AIDS infection because TB accelerates the progression of AIDS by increasing the replication rate of HIV (Goletti D et al. *J Immunol* 157:1271-8, 1996). At the same time, persons co-infected with HIV and TB show rapid progression from infection to active TB disease, indicating that HIV infection accelerates the pathogenicity of TB (World Health Organization [WHO], Tuberculosis Strategy and Operations [TB-HIV], Jan 2001). For *M.tb*-infected persons not infected with HIV, 1 in 10 individuals may develop TB over his or her lifetime; in HIV co-infected individuals with weakened immune systems, 1 in 10 persons may develop TB during the next year. Furthermore, infection with *M.tb* accelerates the progression of AIDS, increasing the replication rate of HIV in *M.tb* co-infected individuals (Goletti D et al. *J Immunol* 157: 1271-8, 1996).

The TB crisis is intensified by the emergence of TB caused by multidrug-resistant *M.tb*. The long duration and associated side effects of standard TB drug treatment often result in patients not completing their full course of therapy. When individuals do not complete their full course of therapy, single- and multidrug-resistant strains of TB may emerge that are more difficult and more expensive to treat. Patients with drug-resistant strains may require up to 2 years of treatment and may remain infectious for longer periods of time compared with patients with non-multidrug-

resistant organisms (CDC. Fact Sheet: Treatment of Drug-Resistant Tuberculosis, June 20, 2000. www.cdc.gov/nchstp/tb/pubs/tbfactsheets/250112.htm).

Drug-resistant TB represents a small percentage of the total cases of TB in the United States, with the most common form being *M.tb* strains resistant to the commonly prescribed TB drug isoniazid. For the more than 85 percent of culture-positive cases in which data on drug resistance were available, resistance to at least isoniazid was between 7 percent and 8 percent in 2002. Among the tested *M.tb* strains, resistance to two of the most commonly prescribed drugs (isoniazid and rifampin) has increased from 116 cases (1.0 percent) in 2001 to 121 cases (1.2 percent) in 2002 in patients who have no prior history of drug-resistant TB (CDC. Surveillance Slides, 2002. www.cdc.gov/nchstp/tb/pubs/slidesets/surv/default.htm).

Over the past decade, NIAID has dramatically boosted funding for TB research. This increased funding has allowed the Institute to support a number of initiatives and a markedly expanded community of TB researchers. Higher levels of funding enabled NIAID to establish the Tuberculosis Research Unit (TBRU) at Case Western Reserve University in 1994 (www.tbresearchunit.org). TBRU conducts clinical trials of potentially new TB therapeutic, preventive, and diagnostic strategies. At the same time, TBRU continues to make progress in developing surrogate markers of disease and human protective immunity. A newly established repository will distribute well-characterized clinical samples to TBRU investigators and their collaborators. TBRU activities are coordinated with major organizations involved in TB research, including CDC, the Food and Drug Administration, the United States Agency for International Development, WHO, Global Alliance for TB Drug Development, and the International Union Against Tuberculosis and Lung Disease, and with interested industrial partners.

NIAID's extramural TB research program currently supports more than 230 grants for basic, applied, and clinical research. Among the projects supported by NIAID is an award to The Institute

for Genomic Research (TIGR) in Rockville, Maryland, to sequence and annotate *Mycobacterium smegmatis* (strain MC2 155), an important model system used in TB research. *M. smegmatis* microarrays also will be produced as part of this grant and are expected to be distributed through the Pathogen Functional Genomics Resource Center in FY 2004. For additional information on genome data, see www.tigr.org/tdb/mdb/mdbinprogress.html.

One of NIAID's high priorities is the development of improved TB vaccines, which are crucial to the long-term control of TB worldwide. NIAID's *Blueprint for TB Vaccine Development*, presented at the 1998 International Symposium for Tuberculosis Vaccine Development and Evaluation, outlines the specific steps needed to develop improved TB vaccines (www.niaid.nih.gov/publications/blueprint). A task force with representatives from NIAID and several Department of Health and Human Services (DHHS) agencies, will oversee the implementation of the report. NIAID's Vaccine Treatment and Evaluation Unit in St. Louis, Missouri, will work with the Global Vaccine Foundation to conduct a phase I safety and immunogenicity trial on a new anti-TB vaccine (recombinant bacille Calmette-Guerin vaccine). This candidate vaccine was originally developed with NIAID grant support. Enrollment in the phase I safety and immunogenicity trial is expected to begin in early spring 2004.

Through the Tuberculosis Research Materials and Vaccine Testing contract at Colorado State University, NIAID provides TB research reagents to qualified investigators throughout the world. The TB research reagents provided by NIAID enable researchers to work with consistent, high-quality reagents prepared from the highly contagious and technically demanding causative *M.tb* pathogen. This contract also screens potential TB vaccine candidates in appropriate animal models. During 2003, 121 individual vaccines or adjuvant candidates have been tested, with 15 vaccine-testing experiments completed, 16 experiments in process, and 7 under development.

The Southern Research Institute in Birmingham, Alabama, maintains an NIAID-supported Tuberculosis Antimicrobial Acquisition and Coordinating Facility (TAACF). TAACF acquires compounds for screening against virulent *M.tb*, maintains a computerized chemical database of compound structures, coordinates and distributes compounds for evaluation *in vitro* and in animal models, and reports data to suppliers. TAACF has contacted more than 3,500 chemists throughout the world seeking candidate anti-TB compounds. More than 60,000 candidate anti-TB compounds have been received from academic and private sector investigators principally in the United States and Europe, with growing involvement of scientists from Africa, Asia, Australia, South America, and other geographic sites. For more information, please visit www.taacf.org.

NIAID's Division of Intramural Research has a substantial intramural program that integrates genomics and combinatorial chemistry to speed the development of new antibiotics for the control of tuberculosis. At present, intramural scientists are working on a number of approaches to improve current anti-TB chemotherapeutics.

Sexually Transmitted Infections

Because of their devastating impact on women and infants and their causal association with HIV/AIDS, sexually transmitted infections (STIs) are critical global and national health priorities. STIs often have severe sequelae such as infertility, tubal pregnancy, cervical cancer, fetal wastage, low birthweight, congenital or perinatal infection, and HIV/AIDS infection. Recent studies indicate that nonulcerative STIs (e.g., chlamydia, gonorrhea, and trichomoniasis) and ulcerative STIs (e.g., genital herpes, syphilis, and chancroid) increase the risk of HIV/AIDS transmission by at least twofold to fivefold. Because HIV/AIDS infection is characterized by a weakened or nonfunctioning immune system, it can alter the natural history of some STIs (e.g., pelvic inflammatory disease and human papillomavirus infection).

Individuals with STIs are at least 2 to 5 times more likely than uninfected individuals to acquire HIV if

they are exposed to the virus through sexual contact. In addition, if an HIV-infected individual also is infected with another STI, that person is more likely to transmit HIV through sexual contact than other HIV-infected persons (CDC. *The Role of STD Detection and Treatment in HIV Prevention*. www.cdc.gov/nchstp/dstd/fact_sheets/facts_std_testing_and_treatment.htm).

Even though rates of some STIs (e.g., syphilis) saw an overall U.S.-wide decline in 2001, a recent report by CDC indicates that STI rates tend to be higher among African Americans than among whites. In 2001, the rate of primary and secondary syphilis reported in African Americans (11.0 cases per 100,000 population) was 16 times greater than the rate reported in whites (0.7 cases per 100,000). This differential was substantially less than that in 1997, when the rate of primary and secondary syphilis among African Americans was 44 times greater than the rate reported among whites. Although STI rates tend to be higher among African Americans than whites, the differential rates between the two groups declined between 1997 and 2001. Declining differences are due to consistent decreases in STI rates in African Americans together with an increase in STI rates in whites (U.S. Trends in Sexually Transmitted Diseases. [all from STD Surveillance, 2001. DHHS, CDC, September 2002 unless otherwise cited])

NIAID supports individual investigator-initiated research grants and a variety of research programs for the development of more effective prevention and treatment approaches to control STIs (www.niaid.nih.gov/dmid/STDs). Research efforts include developing and licensing vaccines, topical microbicides, and treatments for the microbes that cause STIs; understanding the long-term health impact of sexually transmitted pathogens in various populations; stimulating basic research on the pathogenesis, immunity, and structural biology of these pathogens; and developing better and more rapid diagnostics. Specific programs supported by NIAID include the Sexually Transmitted Disease (STD) Cooperative Research Centers (CRCs), which bridge basic biomedical, clinical, behavioral, and epidemiologic research; promote productive

collaborations among academic researchers; and facilitate the development of intervention-oriented research. Another program, the STD Clinical Trials Unit, conducts clinical trials to test the safety and efficacy of biomedical and behavioral interventions aimed at the prevention and control of STIs. Finally, the Topical Microbicides Program Projects conduct basic research, product development, and clinical evaluation activities aimed at developing female-controlled barrier methods for the prevention of STIs and HIV/AIDS infection.

As part of the Public Health Service's effort to eliminate syphilis in the United States by 2005, NIAID's efforts focus on providing better biomedical tools to prevent and control this disease. These efforts include (1) diagnostic test development, which is intended to create a rapid, inexpensive, easy-to-use test that would not require a blood sample; (2) a clinical research study of oral therapy to treat early-stage syphilis; and (3) development of a syphilis vaccine that would target and prevent systemic infection (including congenital syphilis) and could potentially ameliorate disease progression.

NIAID currently is 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, benzathine penicillin G. Azithromycin offers many advantages over benzathine penicillin. Azithromycin is taken orally; benzathine penicillin is administered by often-painful injections that can 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 tuberculosis.

The long-term goals of all NIAID's syphilis activities are to (1) complement CDC's syphilis elimination program, (2) provide improved biomedical and behavioral tools to achieve and

sustain syphilis elimination in the United States, and (3) provide improved tools for prevention and control of syphilis in developing countries. NIAID's research takes into account the limited resources of areas where syphilis is endemic, the social and cultural barriers to accessing effective health care in some of those endemic areas, and the need for sustainable interventions.

In addition, NIAID continues to initiate and support a variety of other STI research projects, including the following:

- Developing and evaluating STI diagnostics designed for point-of-care use through the Small Business Innovation Research mechanism
- Continuing to support grants for the development of vaccines to prevent chlamydial and gonorrheal infections
- Supporting a herpes vaccine efficacy trial
- Supporting an STD CRC focused on preventing STIs. Through this center, two studies will examine strategies for preventing bacterial vaginosis, herpes, and chlamydial infections
- Supporting an STD CRC focused on multidisciplinary research on sexual behavior, clinical epidemiology, immunobiology, and the pathogenesis of gonococcal and chlamydial infections
- Supporting an STD CRC that emphasizes research exploring more effective interventions for preventing STI morbidity in adolescents
- Supporting a longitudinal study to examine social and sexual networks of Hispanic adolescents in San Francisco

NIAID also supports the sequencing of the genomes of sexually transmitted pathogens, including *Chlamydia trachomatis*, *Treponema pallidum*, and *Ureaplasma urealyticum*. Completed

genome sequences have provided new insights into the pathogenesis of their associated diseases and pave the way for new opportunities to develop diagnostics, drugs, vaccines, and microbicides.

Additional activities include the following:

- Opened in November 2002, the Herpevac Trial for Women is a pivotal phase III double-blind clinical efficacy trial of an investigational vaccine for the prevention of genital herpes. The study, conducted as a public-private partnership with GlaxoSmithKline, will enroll 7,550 women at approximately 25 sites across the United States. The trial will require an estimated 4 years to complete.
- This past year, the STDs Prevention Primate Unit for preclinical evaluation of topical microbicides and vaccines at the University of Washington evaluated several candidate microbicides for safety by examining the effects on surface tissues and the impact on the microenvironment of the cervix and vagina in pig-tailed macaques. Results from the testing contract are supported by the Division of Microbiology and Infectious Diseases (DMID). Coordination and testing are conducted in association with the Division of Acquired Immunodeficiency Syndrome (DAIDS). DMID and DAIDS will facilitate product development and ensure safety and efficacy testing in clinical trials.
- The Topical Microbicides Development and Evaluation Workshop, held on March 18–20, 2003, was the first joint meeting of DMID-, DAIDS-, and NICHD-supported investigators conducting research on topical microbicides. The workshop addressed issues ranging from basic research through formulation and applicator design and served as a forum for establishing collaborative work among STI and HIV/AIDS investigators in the microbicide arena.
- The STD Clinical Trials Unit is conducting a randomized phase III trial to evaluate the

equivalency of oral azithromycin versus injectable benzathine penicillin for the treatment of primary syphilis. If successful, this trial may provide an additional antimicrobial strategy for treating primary syphilis.

- Collaborating with STD CRCs, NIAID continues to support a research program with second-year medical students from Howard University in Washington, DC. This program provides students with a 10-week STI research experience at the STD CRCs, with the long-term objective of encouraging young minority physicians to pursue careers in STI research.

Hepatitis C

Hepatitis C virus (HCV) infection is the most common chronic blood-borne viral infection in the United States. HCV infects approximately 2 percent of the U.S. population, or approximately 4 million persons. New infections in the United States continue at the rate of 25,000 cases per year (www.cdc.gov/ncidod/diseases/hepatitis/c/fact.htm). According to CDC, HCV infection occurs among persons of all ages, but the highest incidence rate of acute hepatitis C is found among persons between ages 20 and 40 years, and males predominate. African Americans and whites have similar incidence rates of acute disease. Persons of Hispanic ethnicity have higher rates of acute disease. In the general population, the highest prevalence rates of HCV infection are found among persons in the 30-to-50 age range, and again males predominate. Unlike the rates of acute disease, African Americans have a substantially higher prevalence of HCV infection than do whites.

NIAID has aggressively pursued the expansion of HCV research through its development of the *Hepatitis C Framework for Progress*. With the aid of participating Institutes and Centers, an NIH-wide framework was drafted that incorporates varying individual missions into a cohesive global plan. The final plan underwent external review and has been approved by the NIH Director as well as NIH

Institute and Center Directors. The following research goals were identified in the framework:

- Understanding HCV transmission modes to develop effective intervention strategies
- Understanding HCV pathogenic mechanisms and disease progression to develop effective treatments
- Characterizing hosts' immune responses to HCV infection to develop vaccines, prophylactic measures, and therapeutic measures
- Defining viral replication and recovery with therapy develop new therapeutic strategies
- Investigating clinical manifestations to develop noninvasive methods to evaluate current disease state, to predict outcomes, and to prevent or reverse disease progression
- Defining effective prevention and intervention strategies to improve health

One of the cornerstones of NIAID's HCV effort is the Hepatitis C Cooperative Research Centers (HC CRCs), which were launched in 1996 as basic and clinical research units devoted to understanding HCV infection and disease processes. Currently, NIAID provides funding support to six HC CRCs. The goals of NIAID's six HC CRCs are to identify components of HCV, isolate the body's immune response to HCV, determine the individual genetic factors that have a crucial impact on recovery from initial and chronic infection, track disease progression and severity, and determine how cofactors influence HCV disease. Clinical research emphasizes studies in special populations (e.g., African Americans) heavily affected by HCV that respond poorly to standard therapies. Specifically, one of the HCV CRCs is conducting a therapeutic clinical trial examining the use of pegylated interferon and ribavirin in parallel cohorts of African Americans and whites. The goal of this clinical trial is to determine what causes disparities between African Americans and whites in response to standard therapy.

Other NIAID HCV research activities include the following:

- NIAID continues to provide partial support for the ancillary studies of the NIDDK-sponsored trial, “Hepatitis C Antiviral Long-term Treatment against Cirrhosis (HALT-C).” The trial is evaluating the impact of long-term therapy on disease progression, including virologic and immunologic responses and their association with recovery.
- NIAID supports HCV epidemiological research and treatment trials within its HIV clinical trial networks.
- NIAID research efforts toward the development of vaccines have been and remain primarily focused on developing a better understanding of the molecular biology of HCV and the immune response to HCV infection. These investigations are providing an in-depth analysis of immune responses to HCV infection, the role of cytokines and other immune regulatory molecules in the control of HCV infections, and the evolution of virus in response to the immune response mounted by the host.
- The development of antivirals for HCV has been hindered by the lack of robust and economical cell culture and animal models. NIAID grantees have recently developed a novel enzymatic reporter system for the detection and quantitation of HCV ribonucleic acid in intact cells. This cell-based system was optimized for a high-throughput screening program and is being used to identify new antiviral compounds for HCV.
- Extramural investigators developed HCV cell lines that are now validated as *in vitro* antiviral screening tools. NIAID supports two of these systems via its *in vitro* screening contract programs. These systems are used by academic and corporate scientists (www.niaid.nih.gov/dmid/viral).
- NIAID’s extramural program has initiated two activities to broaden HCV research and

development. The first activity involves the acquisition and provision of HCV research reagents. These reagents are obtainable through the AIDS Research and Reference Reagent Program (www.aidsreagent.org). Other reagents are available through www.niaid.nih.gov/reposit/tetramer/index.html and www.bratonbiotech.com/braton11.htm. The second activity involves the development of an annotated HCV sequence database by Los Alamos National Laboratories (<http://hcv.lanl.gov/content/hcv-db/index>).

- NIAID released the “Liver and Pancreatic Disease in HIV Infection” program announcement (PA), sponsored jointly with NIDDK. This program is intended to stimulate research on the pathogenesis and therapeutics of liver and pancreatic disease associated with the co-infections (e.g., hepatitis B, hepatitis C) that occur in patients with HIV infection. This PA also seeks to stimulate research in the metabolic complications associated with treating HIV infection. Metabolic complications include hepatic drug toxicity, hepatic lipid metabolism, nonalcoholic steatohepatitis, and pancreatitis.
- Researchers supported by NIAID are investigating the relationships between HCV replication, evolution, and disease progression in Alaska Natives. To date, more than 900 HCV-positive patients have been enrolled in the study. Complete patient histories, including the estimated date of infection and alcohol history, are being obtained. Blood and liver specimens are being collected both retrospectively and prospectively. Specimens will be examined to determine the levels and variation of HCV virus and will be compared with the disease progression in patients. This well-defined Alaska Native population may provide many key answers regarding the natural history of hepatitis C and may affect the future worldwide treatment of hepatitis C.

Pneumonia

Pneumococcal pneumonia is an infection in the lungs caused by the *Streptococcus pneumoniae* (*S. pneumoniae* or pneumococcus). Pneumococcus

can infect the upper respiratory tracts of adults and children and can spread to the blood, lungs, middle ear, or nervous system. More than 60,000 cases and more than 6,000 deaths from invasive pneumococcal disease (e.g., bacteremia and meningitis) are estimated to occur annually in the United States. Rates of invasive infection increase with age and are disproportionately higher among certain minority populations. For example, children of Alaska Native ethnicity, those from certain American Indian groups, and children of African American origin have increased rates of pneumococcal pneumonia. Pneumococci account for up to 36 percent of adult community-acquired pneumonia and 50 percent of hospital-acquired pneumonia. Pneumonia is a common bacterial complication of influenza and measles. The pneumonia case-fatality rate is 5 percent to 7 percent and may be much higher in elderly persons (www.cdc.gov/nip/publications/pink/pneumo2.pdf).

NIAID has supported an efficacy and safety phase III randomized trial in 8,292 Navajo and White Mountain Apache children using the licensed 7-valent pneumococcal conjugate vaccine Prevnar. Results of the trial demonstrate that the vaccine is highly efficacious (76.8 percent) against vaccine serotype invasive pneumococcal disease in this high-risk population. The data clearly demonstrate that the vaccine is capable of preventing disease, not only in the general U.S. population, but also in a setting where pneumococcal colonization frequency is 50 percent at 2 months of age.

Acquired Immunodeficiency Syndrome

Since the emergence of HIV/AIDS as a deadly global infectious disease in 1981, considerable progress has been made in understanding the impact of HIV/AIDS on the immune system and how to intervene therapeutically. Researchers have developed new techniques to detect HIV/AIDS in blood and tissue and have also identified powerful new antiviral therapies. These therapies, referred to as HAART, suppress the virus to undetectable levels in the blood and delay disease progression and

death. Since the widespread introduction of HAART, deaths in persons with HIV/AIDS have dropped dramatically in the United States and other developed countries. HIV-infected individuals live longer as a result of HAART, but many experience a host of complications from the complex therapeutic regimen. These complications include the development of drug resistance, metabolic abnormalities and toxicities, and patient noncompliance. Despite the scientific advances, AIDS continues to rage around the world.

According to the Joint United Nations Programme on HIV/AIDS, 42 million people were estimated to be living with HIV/AIDS, and 3.1 million people died from AIDS worldwide in 2002. In addition, 5 million people became infected with HIV in 2002, including 2 million women and 800,000 children aged 15 years and younger.

More than 830,000 cases of AIDS have been reported in the United States since the epidemic began in 1981, with an estimated 384,906 persons known to currently be living with AIDS. One-quarter of the approximately 950,000 Americans who currently may be infected with HIV are unaware of their infection. Although AIDS affects all groups, the disease continues to disproportionately affect racial and ethnic minority populations. African Americans and Hispanics constitute 61 percent of the AIDS cases in the United States. Although African Americans comprise only 12 percent of the U.S. population, they make up almost 41 percent of all AIDS cases reported in the United States. Similarly, Hispanics comprise 13 percent of the U.S. population and represent 19 percent of all AIDS cases. Of the new AIDS cases reported in 2002, 55 percent were among African Americans, 13 percent among Hispanics, and 32 percent among whites; less than 1 percent were among American Indians, Alaska Natives, and Asian-Pacific Islanders. Among women, African Americans and Hispanics account for 81 percent of AIDS cases. Among men, African Americans and Hispanics account for 64 percent of cases. Minority children also are disproportionately affected by AIDS. Of the 92 pediatric AIDS cases reported in 2002, 89 percent (82) were in African American and Hispanic children. CDC reported 16,371

deaths from AIDS in the United States in 2002, of which 52.3 percent were African Americans, 18.7 percent were Hispanics, 27.8 percent were whites, 0.6 percent were Asian-Pacific Islanders, and 0.4 percent were American Indians and Alaska Natives (CDC. *HIV/AIDS Surveillance Report*, Vol.14, 2002. www.cdc.gov/hiv/stats/hasr1402.htm).

The disproportionate impact of the HIV/AIDS epidemic is seen more clearly by comparing the rates of infection between specific groups. Rates of infection are defined as the number of cases per 100,000 people. The rate of HIV/AIDS infection is 5.9 among whites, 58.7 among African Americans, 19.2 among Hispanics, 4.0 among Asian-Pacific Islanders, and 8.5 among American Indians and Alaska Natives.

The estimated number of people living with AIDS at the end of 2002 in 30 areas with confidential name-based reporting show that HIV transmission due to substance abuse continues to be a significant factor in contributing to the spread of HIV/AIDS in minority communities. Data show that 24 percent of African American males and 23 percent of Hispanic males reported injection drug use as a potential exposure route for HIV/AIDS. In contrast, only 10 percent of whites reported injection drug use as a potential for exposure. Among women, injection drug use was reported as a potential exposure route for HIV/AIDS by approximately 24 percent of African Americans, 26 percent of Hispanics, 17 percent of Asian-Pacific Islanders, 36 percent of American Indians and Alaska Natives, and 34 percent of whites. A large proportion of women become infected with HIV/AIDS through sexual contact with an injection drug user. Of the HIV+ women in the United States, more than 75 percent were infected through heterosexual contact. Another factor contributing to the spread of HIV/AIDS in minority communities is men having sex with men (MSMs). For both African American and Hispanic males, MSM continues to be the leading exposure method (CDC. *HIV/AIDS Surveillance Report*, Vol.14, 2002). For the most up-to-date U.S. HIV/AIDS statistics, please visit www.cdc.gov/hiv/stats/hasr1402.htm.

As the HIV/AIDS epidemic continues to expand in minority communities, enrolling minority patients in HIV/AIDS clinical trials is particularly urgent so that research results are applicable to all populations affected by the disease. People of minority backgrounds face unique social, economic, and medical issues when coping with the challenges associated with HIV/AIDS infection, and therefore, one of the greatest challenges facing HIV/AIDS researchers today is the recruitment and retention of minority patients for clinical trials. To ensure that enrollment reflects the national epidemic, NIAID has taken strong steps to encourage minority participation in clinical trials, natural history studies, and prevention studies. NIAID works with communities to identify and overcome barriers to participating in clinical trials. Outreach is accomplished by developing culturally sensitive education materials and providing additional resources (e.g., childcare, transportation) that are necessary for enhancing participation by all communities in NIAID-sponsored trials. NIAID also has taken a leadership role in involving community representatives in local, national, and international research activities. Encouraging community members to play an active role in all aspects of research facilitates communication and helps ensure that new HIV/AIDS treatment and prevention strategies address areas of utmost concern to those affected by the disease. NIAID's HIV/AIDS clinical research networks provide opportunities for community representatives to participate in the research process through local, national, and international Community Advisory Boards. In addition, NIAID recently released the "Enrolling Women and Minorities in HIV/AIDS Research Trials" program announcement. This program will fund innovative approaches to reach, enroll, and retain women and racial/ethnic minorities in HIV/AIDS research trials in the United States. Research trials will be conducted to advance the body of scientific knowledge that will improve the diagnosis, treatment, and development of preventive strategies for women and minorities.

NIAID directs a large therapeutic clinical trials program consisting of three groups: the Adult AIDS Clinical Trials Group (AACTG), the Pediatric AIDS Clinical Trials Group (PACTG), and the Terry

Beirn Community Programs for Clinical Research on AIDS (CPCRA). AACTG investigates therapeutic interventions for HIV infection, AIDS, and complications of HIV-associated immune deficiency in adults (<http://aactg.s-3.com>). PACTG evaluates clinical interventions for treating HIV infection and HIV-associated illnesses in neonates, infants, children, adolescents, and pregnant women. PACTG also researches approaches to prevent mother-to-child transmission (MTCT) of HIV (<http://pactg.s-3.com>). CPCRA is a network of community-based health centers and clinics that support clinical research in community settings. CPCRA conducts large, comparative studies that evaluate therapies and treatment strategies for HIV infection and HIV-associated illnesses (www.cpcra.org). AACTG, PACTG, and CPCRA strive to ensure that a sufficient proportion of minority individuals is enrolled in clinical trials. In 2003, 7,699 and 2,984 participants were enrolled in AACTG and PACTG studies, respectively. In the AACTG, 29 percent were African American, 18 percent Hispanic, 2 percent Asian-Pacific Islander, and less than 1 percent American Indian and Alaska Native. In the PACTG, 57 percent were African American, 28 percent Hispanic, and less than 1 percent Asian-Pacific Islander, American Indian, or Alaska Native. Of the 3,513 patients who were enrolled in CPCRA studies during FY 2003, 46 percent were African American, 16 percent were Hispanic, 0.7 percent were Asian-Pacific Islanders, and 0.5 percent were American Indians and Alaska Natives (NIAID. HIV Infections in Minority Populations, August, 2003. www.thebody.com/niaid/2003/minorities_hiv.html).

NIAID's epidemiologic research explores the clinical course and factors contributing to the transmission of HIV/AIDS infection in a variety of populations. NIAID supports several studies, including the Women and Infants Transmission Study (WITS), which targets inner-city women and their children; the Women's Interagency HIV/AIDS Study (WIHS), which explores the clinical course of HIV/AIDS infection in women with a focus on minority women (<http://statepiaps.jhsph.edu/wihs>); and the Multicenter AIDS Cohort Study (MACS), a prospective, longitudinal study of HIV/AIDS

disease in homosexual and bisexual men (<http://statepi.jhsph.edu/mac/macs>). WIHS and MACS are the two largest observational studies of HIV/AIDS in women and homosexual or bisexual men in the United States. These studies have made major contributions in understanding how HIV is spread, understanding HIV disease and progression to AIDS, and developing the most effective methods for treating HIV/AIDS. As of the completion of the enrollment period, WIHS and MACS have increased the study group size by 60 percent and added to the total number of minority participants. The expanded groups will focus on contemporary questions regarding HIV infection and treatment. This year, MACS is entering its 20th year of research while WIHS has just completed its 10th year of research. In 2003, the enrollment of individuals from minority communities in NIAID-supported epidemiology cohorts was 23.3 percent in MACS, 85.1 percent in WIHS, and 85.4 percent in WITS. MACS is co-funded by the National Cancer Institute (NCI) and the National Heart Lung and Blood Institute. WIHS is co-funded by NCI, NICHD, the National Institute of Dental and Craniofacial Research, and the National Institute on Drug Abuse (NIDA).

Vaccine Development

NIAID continues to support efforts to develop an effective HIV vaccine for use around the world. Established in 2000, the HIV Vaccine Trials Network (HVTN) is a collaboration of domestic and international clinical sites dedicated to developing a preventive HIV vaccine. Building on the previous accomplishments of NIAID's AIDS Vaccine Evaluation Group and the HIV Network for Prevention Trials (HIVNET), HVTN tests and evaluates candidate vaccines in clinical trials. There are 18 sites in the United States and 13 sites overseas, including sites in Africa, Asia, South America, and the Caribbean. HVTN's global capacity will allow for rapid expansion and the ability to perform large-scale studies of suitable vaccines as more vaccine candidates enter the pipeline for testing and development. In 2003, 13 percent of participants in U.S. HVTN studies were African American, 4.2 percent were Hispanic,

1.8 percent were Asian-Pacific Islander, and 1.0 percent were American Indian and Alaska Native.

Currently, HVTN is conducting six phase I and two phase II clinical trials of candidate HIV vaccines. For more information about these trials, please visit www.hvtn.org or www.aidsinfo.nih.gov.

The participation of international sites and the involvement of ethnically diverse populations in HVTN studies are critical components of NIAID's HIV/AIDS vaccine effort. HVTN's broad participation allows researchers to design studies that examine factors crucial to developing an effective vaccine for use around the world. These factors include genetic background, nutritional status, effects of co-infection, and access to health care. HVTN's international capacity also facilitates studies of the HIV/AIDS subtypes, which affect a minority of the global population. Studying HIV/AIDS subtypes is an important aspect of developing a vaccine that will protect individuals from the various circulating strains of HIV/AIDS.

In addition to conducting clinical studies, HVTN develops community outreach programs to educate people about HIV/AIDS and vaccine research. Through outreach, HVTN seeks to encourage participation in clinical trials and enroll a diverse population, emphasizing the recruitment of minorities and women.

NIAID also is actively involved in educating the public about HIV vaccine research and is currently in year two of its HIV Vaccine Communications Campaign. Targeting at-risk populations, in particular African Americans, Hispanics, and MSMs, the NIAID HIV Vaccine Communications Campaign is developing and implementing a national education campaign to increase awareness of and support for HIV vaccine research, especially in at-risk populations. To ensure that community needs are considered, NIAID receives input and guidance from the HIV Vaccine Communications Steering Group, a group of representatives from the community, Federal agencies, pharmaceutical companies, and HIV vaccine advocacy groups. A

key component of the campaign's first year was to engage individuals and organizations representing target audiences and currently involved in HIV/AIDS prevention and treatment efforts. Roundtable discussions were held with leaders in the African American and Hispanic communities to refine strategies and engage participants in materials development, outreach, and other activities. As part of the campaign, a qualitative, comprehensive research effort was conducted including primary research (e.g., 28 focus groups) and secondary research. This past year, a national survey was completed that evaluated the attitudes and knowledge of HIV vaccine research in the general population, as well as in segmented groups of African Americans, Hispanics, and MSMs. Key findings of the survey indicate that large numbers of African Americans and Hispanics believe that a secret HIV vaccine already exists. The survey also reveals that many African Americans and Hispanics do not know that all vaccine trial volunteers are HIV negative and there is no risk of contracting HIV from the vaccines being tested. The HIV Vaccine Communications Campaign is working to correct the misperceptions that exist regarding HIV vaccine trials and, at the same time, provide general information about HIV vaccine research to minority communities. In early 2003, funding will be provided to community-based and national organizations with strong ties to racial and ethnic minority communities to support local and national HIV vaccine research awareness activities, including activities related to HIV Vaccine Awareness Day, which is designated May 18 of each year. In addition, the campaign is conducting an ongoing program aimed at educating minority media about HIV vaccine research so that they can be better prepared to report on key research findings. For more general information about HIV vaccine research, please visit www.niaid.nih.gov/newsroom/mayday/default.htm.

NIAID established the Dale and Betty Bumpers Vaccine Research Center (VRC) at NIH in 2000. This unique venture within the NIH intramural research program uses national and international collaborations with scientists in academic, clinical, and industrial laboratories to conduct research facilitating the rigorous pursuit of effective vaccines

for AIDS and other human diseases. Developing AIDS vaccines is the highest priority of the center. VRC employs a multidisciplinary approach, integrating research from basic and clinical immunology and virology into vaccine design and production. VRC activities target three main priorities: (1) basic research to establish mechanisms of inducing long-lasting protective immunity against HIV and other pathogens that present special challenges to vaccine development; (2) the conception, design, and preparation of vaccine candidates for HIV and related viruses; and (3) laboratory analysis, animal testing, and clinical trials of vaccine candidates.

VRC actively recruits volunteers to participate in phase I clinical trials. VRC seeks to increase minority participation through a process of outreach and education. Recruiting participants from diverse ethnic backgrounds will ensure that all potential stakeholders are included in developing a successful vaccine.

In November 2002, VRC launched a phase I clinical study of a novel DNA vaccine directed at the three most globally prevalent HIV subtypes, or clades. The vaccine incorporates HIV genetic material from clades A, B and C, which cause about 90 percent of all HIV infections around the world. This first multigene, multiclade HIV vaccine to enter human trials marks an important milestone in the search for a single vaccine targeting the U.S. subtypes of HIV and for the clades causing the global epidemic. During the year-long first phase of the trial, conducted at the NIH campus in Bethesda, Maryland, VRC scientists will assess the vaccine's safety and determine whether the vaccine induces any immune response. Expanded tests conducted through HVTN are planned for several domestic sites, as well as sites in Haiti and South Africa.

Prevention

Preventing the transmission of HIV/AIDS is an important aspect of HIV/AIDS research activities. In an effort to reduce the worldwide spread of HIV, NIAID established the HIV Prevention Trials

Network (HPTN) in 2000. HPTN is a global network of clinical trial sites with 9 sites in the United States and 16 international sites in Africa, Asia, Europe, and South America. The network explores a variety of nonvaccine prevention strategies to reduce HIV/AIDS transmission, such as testing and developing biomedical and behavioral intervention programs. Because HIV/AIDS is transmitted through different routes in various populations, developing a variety of HIV/AIDS prevention strategies will have a significant impact on reducing transmission rates and slowing the worldwide spread of HIV/AIDS. In 2003, 9.5 percent of participants in U.S. HPTN studies were African American, 15 percent were Hispanic, 2.6 percent were Asian-Pacific Islander, and 0.7 percent were American Indian or Alaska Native. Besides being sponsored by NIAID, HPTN is co-sponsored by NICHD, NIDA, and the National Institute of Mental Health.

HPTN evolved from HIVNET, a program that conducted phase I, II, and III clinical trials at U.S. and international sites. Building on HIVNET's many accomplishments, HPTN continues to expand the multidisciplinary research agenda established by HIVNET. HIVNET's accomplishments include the discovery of nevirapine as an effective, affordable drug for preventing MTCT of HIV/AIDS in developing countries, and the establishment of the initial safety and acceptability of two new nondetergent microbicides.

The HPTN scientific agenda is divided into the following six main areas of research:

- Evaluating biomedical approaches to prevent MTCT of HIV
- Developing and evaluating topical microbicides to prevent transmission of HIV
- Developing behavioral interventions to help people reduce their risk of exposure to HIV
- Developing interventions to reduce HIV infection resulting from substance use

- Evaluating programs to control or reduce STIs as a means of decreasing the risk of acquiring and transmitting HIV infection
- Evaluating the impact of antiretroviral therapies in reducing the infectiousness of individuals infected with HIV

Educating communities about HIV/AIDS prevention trials and building community trust has been an important and crucial aspect of HPTN and HVTN outreach. HPTN invites community members to participate in developing its scientific agenda to promote information exchange and ensure that social, cultural, and political values are respected. Community members discuss study designs, recruitment plans, volunteer incentives, informed consent requirements, risk-reduction strategies, and research findings. Each HPTN site also has a community educator who assists community members in understanding the science of HIV/AIDS, research methods that will be used, and the clinical trial process. Community educators build community trust by creating open forums allowing for candid conversations about community fears and concerns related to Government-sponsored research. For information regarding HPTN studies, please visit www.hptn.org or www.aidsinfo.nih.gov.

For more information on HIV/AIDS clinical trials, please visit www.aidsinfo.nih.gov or call 1-800-448-0440.

NIAID Outreach Activities

Disseminating research results to the media, health professionals, and the public is an important aspect of NIAID's mission. Outreach activities include producing and publicizing print, audiovisual, and Web-based materials; distributing materials at professional and community meetings; and sponsoring workshops and conferences for community health care providers and the public.

NIAID produces materials on allergic and immunologic diseases, AIDS/HIV, sexually transmitted infections, and potential illnesses

caused by agents of bioterrorism. Press releases, information sheets, and booklets are distributed worldwide in response to more than 10,000 requests from people who contact NIAID each year. For example, the TB educational booklets *Learn About Tuberculosis/Aprenda Sobre la Tuberculosis* and *Learn About Tuberculosis Infection/Aprenda Sobre la Infeccion de la Tuberculosis* remain popular and are distributed in English and Spanish each year. In addition, the NIAID Web site is visited 1.5 million times each month. Hundreds of thousands of inquirers request materials or download information from the NIAID Web site each year (www.niaid.nih.gov).

Expanding its outreach efforts, NIAID keeps more than 400 voluntary and scientific organizations updated about Institute activities. Periodic e-mails provide NIAID research news and information on advances that specifically relate to an organization's research interests. In addition, workshops on HIV vaccine research were featured at the AIDS Vaccine 2002 conference, the Conference on Retroviruses and Opportunistic Infections, the U.S. Conference on AIDS, the National AIDS Treatment Advocates Forum, the National Association of People With AIDS Conference, and many other scientific and community-oriented conferences. NIAID provides exhibit booths at scientific, health-related, and student scientific organization meetings and conferences where staff distribute materials about allergic, immunologic, and infectious diseases. Staff members working in the booths also answer questions about NIAID research and job opportunities. NIAID performs outreach at conferences sponsored by the following organizations: the American Academy of Allergy, Asthma and Immunology; American Society for Microbiology; American Indian Science and Engineering Society; Hispanic Association of Colleges and Universities; American Public Health Association; Society for Advancement of Chicanos and Native Americans; and Congressional Black Caucus. NIAID has also provided outreach at the Annual Black Family Reunion, the Annual Biomedical Research Conference for Minority Students, and the National Conference on Blacks in Higher Education.

NIAID has been involved extensively in the outreach efforts of the Dale and Betty Bumpers VRC. As VRC prepares for its second HIV vaccine trial, NIAID is helping to construct community partnerships by targeting local news media, visiting local churches and other community organizations, and attending HIV/AIDS-related conferences and meetings.

Working directly with the public is one aspect of NIAID's outreach campaign. NIAID offers a public-speaking component consisting of researchers who will speak on request to community groups and at public schools. NIAID also has participated in a community awareness program addressing cancer awareness, self-management techniques for asthma sufferers, and the silent damage done to the body by hypertension. Staff members have participated as judges in science fair projects at local schools. Working in local schools provides NIAID staff with the opportunity to interact with teachers, parents, and budding scientists.

In FY 2003, NIAID held its first Health Disparities Symposium titled "Increasing Diversity in Clinical Trials: Best Practices." The symposium objectives were the following:

- Examine cultural issues that affect the recruitment and retention of minority participants in clinical trials
- Provide researchers, outreach workers, and community educators with effective strategies for outreach, recruiting, and retaining participants from minority populations
- Demonstrate best practices for using electronic resources to identify applicable clinical trials, human subjects policies, and funding sources and mechanisms

The 200 symposium attendees included NIAID grantees, members of advocacy groups, community physicians, nurse practitioners, and research clinicians. The proceedings of the symposium will be posted on the NIAID Web site at a future date.

II. Minority Researchers' Training and Enhancement Programs

NIH-Wide Programs

Minority Biomedical Research Support Program

Through innovative programs and outreach efforts, NIH continually works to increase the number of minority researchers in the field of biomedical research. The Minority Biomedical Research Support Program (MBRS) is one of the largest NIH programs working toward this goal. MBRS awards grants to educational institutions with substantial minority enrollment. Grants are given to support faculty research, strengthen an institution's biomedical research capabilities, and increase the interest, skills, and competitiveness of students and faculty in the pursuit of careers in biomedical research. NIH Institutes contribute money to the National Institute of General Medical Sciences (NIGMS), which administers MBRS through its Division of Minority Opportunities in Research (www.nigms.nih.gov/about_nigms/more.html#mbrs).

A recent reorganization of MBRS raised the number of institutions that are eligible for research and institutional development support because of their substantial minority student enrollment. Along with this increase, there also has been a rise in the average size of requested grant awards, making these grants comparable in size to other NIH research grants. There are three subcomponents of MBRS: the Support of Continuous Research Excellence (SCORE) initiative, the Research Initiative for Scientific Enhancement (RISE), and the Initiative for Minority Student Development (IMSD).

Collectively, SCORE, RISE, and IMSD provide support from the undergraduate level to the postdoctoral level in institutional development, student and faculty training, and student and faculty career development. Overall program goals for SCORE, RISE, and IMSD are to enhance the science curricula and faculty research capabilities at institutions with significant underrepresented

minority enrollment, encourage minority students to pursue training for scientific careers, and strengthen the research skills of minority students and faculty. The opportunities provided by these programs encourage participation from institutions ranging from 2-year colleges to research-intensive institutions with doctoral programs.

SCORE provides financial assistance to competitive research programs in all areas of biomedical and behavioral research. Funding is provided to develop biomedical research faculty committed to improving competitive research programs and increasing the number of underrepresented minorities professionally engaged in biomedical research. The program supports faculty-initiated, scientifically meritorious research projects, including pilot research projects (<http://grants1.nih.gov/grants/guide/pa-files/PAR-04-001.html>).

RISE seeks to enhance the research environment at minority-serving institutions through faculty and student development by increasing the interests, skills, and competitiveness of students and faculty who are pursuing biomedical research careers. RISE offers support for faculty and student development activities such as on-campus workshops, off-campus workshops, specialty courses, travel to scientific meetings, and research experiences at on-campus or off-campus laboratories. Support also is available for evaluation activities and limited institutional development (e.g., equipment purchases, the development of research courses, the renovation or remodeling of existing facilities to provide space for an investigator to conduct developmental activities) (<http://grants.nih.gov/grants/guide/pa-files/PAR-99-151.html>).

IMSD encourages domestic private and public educational institutions with fully developed and funded research programs to initiate and/or expand innovative programs to target underrepresented minority students. Institutions that receive the funding are expected to improve the academic and

research capabilities of underrepresented minority students and to facilitate their progress toward careers in biomedical research. Funding also may be directed toward developing underrepresented minority scientists who are in any phase of their career development, from the undergraduate level through the Ph.D. level. IMSD awards use the institutional education project grant mechanism (<http://grants1.nih.gov/grants/guide/pa-files/PAR-02-084.html>).

Minority Access to Research Careers

The Minority Access to Research Careers (MARC) Undergraduate Student Training in Academic Research (U*STAR) program provides support for students who are members of minority groups that are underrepresented in the biomedical sciences at institutions with significant minority student enrollments. U*STAR seeks to improve students' preparation for graduate training in biomedical research through faculty development, strengthening of science course curricula, development of biomedical research training programs, and infrastructure development. Additional information about this program is available online at <http://grants1.nih.gov/grants/guide/pa-files/PAR-02-033.html>.

MARC predoctoral fellowships provide funding for graduates of the U*STAR program. The program provides outstanding U*STAR students with up to 5 years of support for research training leading to a Ph.D., M.D./Ph.D., or other combined professional degree/Ph.D. in the biomedical or behavioral sciences, including mathematics. Support is available only for individuals enrolled in a combined professional degree/Ph.D. program in the biomedical or behavioral sciences. The MARC predoctoral fellowship program encourages students from minority groups underrepresented in the biomedical and behavioral sciences to seek graduate degrees. This program furthers the NIH goal of increasing the number of underrepresented minority scientists who are competitively trained to pursue careers in biomedical or behavioral research. For more details on these fellowships, visit <http://grants2.nih.gov/grants/guide/pa-files/PAR-03-114.html>.

MARC faculty predoctoral fellowships are awarded to faculty members of colleges or universities with significant minority enrollment. Awards provide eligible faculty lacking a Ph.D. degree or Ph.D. equivalent the opportunity to obtain a research doctorate. Applicants must be full-time, permanent faculty in a biomedical science or mathematics program and must have been at the minority institution for at least 3 years at the time of application. Candidates must be enrolled in or have been accepted into a Ph.D. or combined M.D./Ph.D. training program in the biomedical or behavioral sciences at the time of application. Applicants also must state their intention to return to the minority institution at the end of their training period. Additional information on faculty predoctoral fellowships is available at <http://grants2.nih.gov/grants/guide/pa-files/PAR-03-048.html>.

MARC faculty senior fellowships are awarded to eligible faculty members of colleges or universities with significant minority enrollment. The goal of the fellowship is to provide eligible faculty members a yearlong period of intensive research in a state-of-the-art research environment to update their research skills or move into new areas of research. Applicants must be full-time faculty members in a biomedical science or mathematics program for at least 3 years at the time of application. Moreover, candidates must have received a Ph.D. or Ph.D. equivalent at least 7 years before the date of application. Candidates must state their intention to return to the minority institution at the end of their training period. Applicants must request support ranging from 1 academic year (e.g., 9 months) to 2 years. Additional information is available online at <http://grants1.nih.gov/grants/guide/pa-files/PAR-02-145.html>.

Research Supplements for Underrepresented Minorities Program

In 1989, NIH launched an initiative to provide funding for underrepresented minorities in biomedical research at all levels of career development. The Research Supplements for Underrepresented Minorities (RSUM) program seeks to increase the number of underrepresented minorities in biomedical research. RSUM

accomplishes its mission by supplementing research grants currently funded by NIH Institutes and Centers. Investigators with an existing NIH grant may apply for supplemental funds from RSUM to support minority high school, college, postgraduate, postdoctoral, or junior faculty researchers to work in an area closely allied to the funded research. Awards may be tied to the length of the parent grant and are limited to a total award period not to exceed 4 years.

RSUM defines underrepresented minorities as African Americans, Hispanics, American Indians and Alaska Natives, and Asian-Pacific Islanders. Funds are provided for salary, tuition, fees, expendable supplies, travel, and other incidentals. Award levels are determined by the targeted educational strata, with smaller awards made to high school students. Salary stipends depend on the level of experience and are consistent with the salary scales provided to investigators at the same level of experience in the grantee institution.

In fiscal year (FY) 2003, NIAID funded 41 new and continuing RSUM applications for a total of 6 million dollars. Awardees included minority investigators at the junior faculty, postdoctoral, predoctoral, undergraduate, and high school levels. RSUM promises to be a continued success in increasing the total number of underrepresented minorities in biomedical research in areas of science relevant to NIAID's mission. For more information, please visit www.niaid.nih.gov/facts/mwhhp5.htm#C.

Research Centers in Minority Institutions

NIAID continues to work toward its goal to expand the national capability for health sciences research through the Research Centers in Minority Institutions (RCMI) program. RCMI provides grant support to predominantly minority health professional schools and graduate institutions that offer a doctorate in the health professions or health-related sciences. The program assists institutions in strengthening and augmenting their

human and physical resources for conducting biomedical or behavioral research. RCMI also fosters faculty expansion and development, infrastructure improvement, and the support of research-related activities, including laboratory renovation and equipment replacement. Through RCMI, institutions become more competitive in seeking funding for biomedical or behavioral research. Institutions that qualify to receive RCMI support must have more than 50-percent minority student enrollment and be chartered to award M.D., D.V.M., D.D.S., or Ph.D. health science degrees. Currently, 17 institutions participate in the RCMI program.

RCMI's HIV/AIDS Infrastructure Initiative seeks to ensure that minority institutions have the physical facilities and faculty competence to participate in mainstream HIV/AIDS research. Support is awarded to expand physical infrastructure and improve faculty competence in virology, immunology, molecular biology, and the neurosciences. Participating institutions are located in communities in which the HIV/AIDS epidemic has hit the hardest. As a result, these institutions are uniquely suited to treat and recruit patients in clinical trials. Nine minority medical schools are eligible to participate in the HIV/AIDS Infrastructure Initiative: Howard University, Meharry Medical College, Morehouse School of Medicine, University of Puerto Rico Medical Sciences, Morgan State University, Universidad Central del Caribe, Ponce School of Medicine, Charles R. Drew School of Medicine and Science, Texas Southern University, University of Hawaii, and City University of New York.

RCMI is co-funded by NIAID and the National Center for Research Resources. NIAID provides support for RCMI HIV/AIDS research pilot projects, as well as support for infrastructure development. In FY 2003, NIAID awarded pilot projects for clinical research, molecular vaccine development, opportunistic infections, and immunologic research to seven institutions.

NIAID Programs

Office of Special Populations and Research Training

The Office of Special Populations and Research Training (OSPRT) was established by NIAID's director in 1998 to combine the functions formerly housed in the Office of Research on Minority and Women's Health (ORMWH) and the Office of Science Training and Manpower Development (OSTMD). Combining the functions of OSTMD and ORMWH under one entity has led to greater efficiency in developing research and training initiatives. OSPRT administers the Introduction to Biomedical Research Program (IBRP) and the Bridging the Career Gap for Underrepresented Minority Scientists workshop and serves as NIAID's coordinator and liaison for the Institute's *Strategic Plan for Addressing Health Disparities*. In addition, OSPRT plays a key role in reporting data about women and minority inclusion in phase III clinical trials.

OSPRT's director has been instrumental in overseeing collaborative funding efforts between NIAID, the Center for Minority Health and Health Disparities, and the Office of Research on Women's Health. OSPRT supports innovative programs, such as the Inter-American College of Physicians and Scientists, National Hispanic Youth Initiative, and the Temple University Longitudinal Program.

Bridging the Career Gap

To increase the number of underrepresented minority investigators in biomedical research, the Bridging the Career Gap for Underrepresented Minority Students initiative was established in 1993. Targeting individuals who receive NIAID minority training and research supplemental awards, Bridging the Career Gap seeks to provide young, minority investigators with the tools and information needed for a successful career in biomedical research. The initiative consists of a 2-day seminar addressing career choices, networking, the importance of selecting the right mentor, and the NIH grant system and

components. The seminar also provides participants with the opportunity to network with NIAID intramural and extramural staff. NIAID staff continue to work closely with many students throughout various phases of their careers. The Bridging the Career Gap program demonstrates NIAID's interest in the academic future of its minority training and research supplemental funding awardees. NIAID continues to develop innovative programs that will attract underrepresented minority scientists to the Institute's research agenda.

Results from NIAID's 1996 evaluation of the first two Bridging the Career Gap program cohorts illustrate the program's success. Survey results show that the seminar has many benefits including helping participants understand what to expect from careers in biomedical research and assisting individuals to determine what adjustments are needed in their current career direction to pursue futures in biomedical research; it also provides participants with the opportunity to establish important NIAID contacts. The success of NIAID's Bridging the Career Gap program also has been validated through its replication in other NIH Institutes. The program is administered by OSPRT and is conducted with the assistance of NIAID scientific review, program, and grants management staff and with scientific and administrative experts from academia and industry aligned with NIAID. The sixth Bridging the Career Gap symposium was held in November 2003 and was attended by 70 individuals.

Centers for AIDS Research

NIAID promotes the development of minority scientists in HIV/AIDS research through Centers for AIDS Research (CFARs). CFARs support a multidisciplinary environment promoting basic, clinical, behavioral, and translational research in the prevention, detection, and treatment of HIV/AIDS infections. CFARs accomplish their mission through outreach, fostering scientific communication, training, and sponsoring education. NIAID-sponsored CFARs are committed to educating and training minority

investigators, as well as providing outreach to minority communities.

NIAID Enhancement Award

Historically, NIAID has supported a variety of programs seeking to encourage underrepresented minority investigators to pursue careers in biomedical research. Programs have targeted students ranging in age from high school to postdoctoral levels, and, although these programs have demonstrated success in specific areas, only a few underrepresented minority investigators have become well established in biomedical research. The NIAID Enhancement Award for Underrepresented Minorities was established in FY 2003 to recruit talented underrepresented minority investigators in the early stages of their scientific careers (e.g., assistant professor or junior-level faculty) for basic or clinical research programs in the areas of allergy, immunology, transplantation, microbiology, and infectious diseases, including AIDS. The present Request for Applications is intended to increase the number of underrepresented minority investigators capable of performing independent competitive research and to enhance the long-term research skills and potential of these individuals in all of NIAID's scientific research areas. For more information, please look on the Web at <http://grants1.nih.gov/grants/guide/rfa-files/RFA-AI-03-045.html>.

NIAID/Mali Medical School Minority Training Initiative

In early 1997, the NIAID Division of Intramural Research (DIR), the University of Mali Medical School, and the University of Maryland School of Medicine created a program to provide training opportunities for minority students and young faculty in Africa. NIAID/Mali Medical School Minority Training initiative seeks to provide opportunities that will attract minority students and young faculty to careers in tropical medicine. As a part of the program, American students train in malarial research under Malian researchers at the Malaria Research and Training Center (MRTC) in Bamako, Mali. In turn, Malian researchers are

given sabbaticals to learn new research techniques at NIAID.

In December 1998, the Guest House, located on the campus of the National School of Medicine of Mali and immediately adjacent to MRTC laboratories and the National Medical Library of Mali, was completed. Consisting of a living room, dining, room, kitchen, computer room/library, and eight bedrooms, the Guest House serves as the base of operations for the training program. Each bedroom is equipped with its own computer while the computer room/library has two computers linked to the medical school local area network and the Internet. To ensure student safety, the Guest House is situated within the medical school complex and surrounded by an additional wall staffed by a night guard. Although Mali is generally considered one of the safest countries in Africa, the routine safety precautions are in place to reassure parents and students.

MRTC provides an intricate training program that can accommodate the various educational levels of student participants (e.g., advanced undergraduate students, graduate students, postdoctoral fellows, junior faculty, midcareer faculty) with a potential interest in tropical medicine research. Medical students, recent medical graduates, junior medical faculty, and midcareer faculty are given the opportunity to participate in medical school field training programs, laboratory work, and field work.

The training program emphasizes field research and provides opportunities for all students to work in local villages. As NIH prepares Mali to be a major test site for malaria vaccines, MRTC program participants will have an opportunity to take part in this important and exciting initiative.

In May 1998, the University of Maryland School of Medicine received funding through the Fogarty International Center to manage the promotion, recruitment, selection, and posting of students and fellows in Mali. In FY 2003, a total of 10 students were enrolled in the program, including 2 African Americans, 5 whites, and 3 Asian-Pacific Islanders.

Introduction to Biomedical Research Program

The NIAID IBRP was established in 1979 to inform academically talented college juniors, graduating seniors, and first-year graduate or medical students from underrepresented minority groups about career opportunities in the broad field of biomedical research. This initiative grew out of the need to increase the number of minority scientific researchers in this country. While the numbers of underrepresented minorities in the life sciences has increased, their numbers are still small; to meet the continuing challenge of attracting this population, the program was divided into two distinct programs in 2003. The Richard M. Asofsky Scholars In Research (ASIR) is the IBRP extramural arm and is administered through OSPRT. The intramural arm of IBRP is known as the Introduction to NIAID Research Opportunities (INRO) and is administered through the Division of Intramural Research's Office of Special Emphasis. For more information, please visit www.niaid.nih.gov/ibrp.

Richard M. Asofsky Scholars In Research

For 37 years, Dr. Richard M. Asofsky served NIH and NIAID in improving research training programs. The ASIR program was created in honor of Dr. Asofsky to bring underrepresented minorities into the biomedical sciences. ASIR provides supplemental funding to NIAID extramural principal investigators to conduct laboratory research with underrepresented minority high school and college students. Students gain a mentoring relationship and are exposed to research career opportunities in the areas of allergy, immunology, transplantation, microbiology, and infectious diseases, including AIDS. In FY 2003, 19 students were supported by five NIAID grantees.

Intramural NIAID Research Opportunities Program

Recently, NIAID's Office of Special Emphasis Programs launched the INRO program to encourage committed and talented underrepresented minority students to consider careers in allergy, immunology, and infectious disease research. Undergraduate and first-year

graduate students with a GPA of 3.5 or better were selected to participate in the program based on their interest in NIAID research and their desire to conduct research at the NIH. To qualify for the program, applicants also must be American citizens or legal U.S. residents. In FY 2003, 12 students attended the 3-day intramural program representing colleges and universities from across the United States, Puerto Rico, and the U.S. Virgin Islands. The 3-day program focused on the breadth of research conducted at NIAID and included scientific lectures by intramural researchers, discussions with scientists, and tours of the laboratories in the Research Technology Branch and the Vaccine Research Center. Students also discussed training opportunities with scientists who conduct research in Rockville, Maryland, and the Rocky Mountain Laboratories in Hamilton, Montana. For more information, please visit www.niaid.nih.gov/dir/inro/default.htm.

Temple University Longitudinal Program

In FY 2001, NIAID collaborated with the National Institute of Diabetes and Digestive and Kidney Diseases and the National Institute of Arthritis and Musculoskeletal and Skin Diseases to establish the Temple University Minority Access to Biomedical Research Careers initiative at Temple University in Philadelphia. The initiative is a longitudinal program that recruits outstanding middle school students and provides them with additional instruction in mathematics and the sciences. The goal of this initiative is to increase the pool of M.D./Ph.D. program applicants by ensuring that students succeed in high school and continue in their education to obtain graduate degrees. Participating students are extremely motivated, have research experience, and have very strong academic records. During the summer of their junior and senior years of high school, participants are placed in NIAID intramural laboratories for an 8-week rotation. When participants enter college, the 9-week summer experiences are rotated among Federal, private, and academic institutions.

Participating students assist in research projects, and many of them have been cited in research publications. In FY 2002, 207 students were

participating: 148 African Americans, 32 Asians-Pacific Islanders, and 27 Hispanics. NIAID will continue to support this initiative through FY 2005.

Partnership Program

The Partnership Program continues to benefit NIAID and participating schools. As part of the Partners in Education Program, students are exposed to a scientific environment and are given the opportunity to see science in action, meet and consult with working scientists, gain practical experience by participating in laboratory work, and receive supplemental instruction. Students' interests in the sciences are nurtured through the education program as they improve their understanding and knowledge of biomedical research. Additional resources include monthly lectures, mentoring, role models, tutorial matching, library resources, incentive awards, workplace tours, faculty enrichment, and advisory services. Participating schools also have received NIAID-donated computers, fax machines, microscopes, and numerous laboratory supplies for their science classrooms.

Six schools participated in the Partnership Program in FY 2003. NIAID has partnership agreements with three high schools and three elementary schools: Dunbar High, Friendly High, Crossland High, Ideal Academy, St. Thomas More, and Carmody Hills.

Biomedical Research After School Scholars

Since 1998, scientists from NIAID's Rocky Mountain Laboratories (RML) in Hamilton, Montana, have teamed up with local middle and high schools to present the Biomedical Research After School Scholars (BRASS) program. BRASS introduces 7th- through 12th-grade students to the fundamentals and relevance of biomedical research to stimulate student interest in science and encourage students to pursue careers in biomedical research. The program encourages a broad range of student participation, from minorities, young women, economically disadvantaged, and at-risk students.

BRASS consists of five 2-hour laboratory sessions covering hematology, genetics, cancer, infectious diseases, and animal research. Each 2-hour session is highly interactive, with scientists providing background on topics using the scientific method. The program concludes with a commencement ceremony featuring a guest speaker and laboratory demonstrations conducted by the students.

More than 60 scientists and 350 students have participated BRASS. RML scientists have worked with middle schools in Montana, including Hamilton, Corvallis, Victor, Darby, Stevensville, and Lone Rock middle schools. A March 2003 regional newspaper article, written by students from Lone Rock middle school, can be found at www.missoulian.com/articles/2003/03/17/export3781.txt.

In 2000, RML expanded BRASS to schools located in American Indian and Alaska Native communities. During the past 3 summers, 45 scientists have participated in the Pathways to Academic Excellence (PACE), a mini-BRASS program at an American Indian and Alaska Native summer math and science camp. More than 150 American Indian and Alaska Native students have participated in the minicourse.

Collaborative Efforts

Native American Research Centers for Health

In FY 2001, NIGMS and the Indian Health Service developed the Native American Research Centers for Health (NARCH) program. NARCH supports the development of partnerships composed of American Indian and Alaska Native tribes or tribal-based organizations (e.g., the National Indian Health Board, Local Area Health Boards) and institutions conducting intensive, academic-level, biomedical and behavioral research. The purpose of NARCH is to (1) encourage competitive research linked to reducing health disparities, (2) develop a cadre of American Indian and Alaska Native scientists and health professionals engaged in biomedical, clinical, and behavioral research who will be able to compete for NIH funding, (3) increase the collaborative efforts of research-

intensive institutions and American Indian and Alaska Native organizations and (4) reduce American Indian and Alaska Native community skepticism toward Government-funded research. NARCH continues to support research, student development, and faculty development projects.

As a part of NARCH, NIAID supports two studies that will investigate adult pneumococcal infections in Alaska Natives and White Mountain Apaches. Support for these two studies will continue through FY 2005 and is anticipated to continue through FY 2006.

Interamerican College of Physicians and Scientists

Increasing the participation of underrepresented minority investigators in virtually all fields of biomedical research is a continuing NIH and NIAID priority. NIAID supports a variety of minority programs for biomedical research, from high school through postdoctoral training. NIAID's OSPRT is engaged in an extensive outreach campaign targeting colleges, universities, medical centers, and professional organizations to encourage the participation of minority investigators in NIAID research activities. The Interamerican College of Physicians and Scientists (ICPS) is one outreach activity supported by OSPRT that targets a specific underrepresented community. Founded in 1979, OSPRT promotes cooperation among U.S. Hispanic physicians and seeks to advance their professional and educational development. ICPS is the only national organization representing Hispanic physicians.

The official ICPS journal, *MEDICO Interamericano*, is distributed monthly to 39,000 physicians in the United States. *MEDICO Interamericano* provides information on grants and contracts, as well as information on professional opportunities for Hispanics in academia, Government agencies, and the private sector. ICPS outreach capabilities help increase Hispanic student participation in biomedical research, educate communities regarding minority health issues, and explain NIAID's role in addressing minority health issues through research and other

activities. NIAID continues to provide funding to the ICPS National Hispanic Youth Initiative in Health (NHYI) summer program. NHYI introduces Hispanic youth to careers in biomedical research through scientific seminars and field trips. NHYI motivates, prepares, and encourages Hispanic high school juniors and seniors to pursue careers in health sciences.

Association of American Indian Physicians National Native American Youth Initiative

Through its cooperative agreement with the Office of Minority Health, the Department of Health and Human Services' Association of American Indian Physicians (AAIP) offers a health, biomedical research, and policy development program for American Indian and Alaska Native students between ages 16 and 18 years. AAIP seeks to motivate American Indian and Alaska Native students to remain in school and pursue careers in health professions and/or biomedical research. The National Native American Youth Initiative (NNAYI) prepares American Indian and Alaska Native students for admission to college and professional schools by empowering students with effective leadership skills, analytical skills, and academic proficiency. Promoting self-awareness, NNAYI educates students regarding health status, health care research issues, and policies and legislation that affect American Indian and Alaska Native communities. NNAYI is an intense academic enrichment and reinforcement program consisting of mini-block courses addressing leadership, communication, study skills, testing skills, assertiveness, networking, professional behavior, interactive learning, and time management. Courses are designed to increase students' skills so they are better prepared to remain in school and pursue a career in the health professions and/or biomedical research. The summer program introduces students to the variety of health careers available to American Indian and Alaska Native youth. AAIP members, health professionals, and traditional healers provide a personal perspective for students by relating their experiences in health careers to their familiarity with collaborative efforts between Western and traditional medicine.

III. Future Plans

Allergy, Immunology and Transplantation

NIAID will continue to work toward meeting its goals of increasing efforts in the areas of allergy, immunology, and transplantation that target minority populations and their health care. These plans include the following:

- Through the Immune Tolerance Network and the Autoimmunity Centers of Excellence, NIAID will continue to support clinical trials and assay development for promising tolerance induction and immunomodulatory strategies to treat asthma and allergic diseases; autoimmune diseases, including systemic lupus erythematosus and scleroderma; and rejection of transplanted organs, tissues, and cells.
- The NIAID Inner-City Asthma Consortium will launch three protocols in 2004, including a cockroach allergen standardization protocol, a study to evaluate the usefulness of measuring exhaled nitric oxide in the clinical management of asthma in children, and a birth cohort to investigate factors that contribute to the development of asthma in inner-city children.
- NIAID will sponsor a workshop at the 2004 annual meeting of the American Academy of Asthma, Allergy and Immunology focusing on the influence of allergens on asthma severity and asthma interventions in inner-city children.
- NIAID plans to sponsor a symposium at the 2004 annual meeting of the American Thoracic Society highlighting recent results of the NIAID National Institute of Environmental Health Sciences' Inner-City Asthma Study.
- In 2004, NIAID will launch the Clinical Trials in Organ Transplantation program. The new program will support a cooperative, multisite consortium for interventional or observational clinical studies, accompanied by mechanistic

studies, to research the immune-mediated pathologic processes in organ transplantation. The consortium will work toward understanding immune-mediated morbidity and mortality of organ transplantation and will seek to develop strategies that will reduce organ transplantation morbidity and mortality.

- In 2004, NIAID will launch the Genomics of Transplantation Program. The new program will establish cooperative interdisciplinary research programs for large-scale, broad-scope genomic studies in clinical transplantation, including solid organ, tissue, and cell transplantation. The goals of this program are to identify and characterize gene polymorphisms and gene expression patterns in immune responses relating to the onset and severity of acute and chronic graft rejection, responses to immunosuppressive therapeutics, and variability in graft survival among populations.

Microbiology and Infectious Diseases

NIAID plans to continue its multidisciplinary microbiology and infectious disease strategies through basic research, targeted studies, and developing innovative vaccine delivery techniques for diseases and infections that disproportionately affect minority populations. Support for investigator-initiated research in areas related to minority health will remain a priority. Plans include the following:

- Support for investigator-initiated, tuberculosis (TB) basic and applied *Mycobacterium tuberculosis* (*M.tb*) research will remain a priority. NIAID seeks to add to the fundamental base of knowledge about *M. Tb* and the pathogenesis of TB to develop improved diagnostic, therapeutic, and intervention strategies for combating TB. NIAID's Division of Microbiology and Infectious Diseases considers the development of improved TB vaccines, drugs, and diagnostics a high priority.

- NIAID's Division of AIDS will continue to support research to discover new, more effective, selective therapeutic agents to treat and prevent TB through screening contracts, investigator-initiated grants, the National Cooperative Drug Discovery Groups for the Treatment of Opportunistic Infections Associated with AIDS program, and Small Business Innovation Research/Small Business Technology Transfer mechanisms.
- NIAID will continue funding basic and clinical research studies on mechanisms of pathogenesis and immunology of bacterial and viral sexually transmitted infections.
- NIAID will continue to support investigator-initiated basic and clinical research for hepatitis C virus. Multidisciplinary research approaches will be encouraged.
- NIAID is exploring the possibility of developing diagnostic assays that can quickly differentiate between bacterial and viral respiratory infections. NIAID also is exploring the possibility of identifying the virulence genes associated with lung tissue that can specifically recognize pneumococcal infections using sputum samples.
- NIAID continues to support efforts to examine new, alternative approaches for improving the diagnosis of community-acquired pneumonia.
- NIAID will continue to support grant supplements to attract underrepresented minority investigators into biomedical and behavioral research through the Research Supplements for Underrepresented Minorities (RSUM) program.
- NIAID will continue to support the Adult and Pediatric AIDS Clinical Trials Group, Terry Bein Community Programs for Clinical Research on AIDS, HIV Vaccine Trials Network (HVTN) and HIV Prevention Trials Network (HPTN). Efforts will continue to increase the participation of women and underrepresented minorities in HIV/AIDS clinical trials.
- NIAID will continue to develop and implement the HIV Vaccine Communications Campaign. In addition, NIAID will continue to coordinate activities surrounding the observance of HIV Vaccine Awareness Day on May 18. Please visit www.niaid.nih.gov/newsroom/mayday/default.htm for more information.
- NIAID will continue to fund the Centers for AIDS Research program.
- NIAID will study the scope and relevance of viral and human genetic variation in relation to vaccine development through HVTN and collaborative efforts with other scientists.
- NIAID will continue to fund the Multicenter AIDS Cohort Study and the Women's Interagency HIV Study epidemiologic cohorts.

Acquired Immunodeficiency Syndrome

NIAID will continue developing innovative strategies to augment minority participation in HIV/AIDS clinical trials and epidemiologic studies. Encouraging the participation of minority investigators in all facets of basic and clinical HIV/AIDS research remains a high priority for NIAID. Specific plans include the following:

- NIAID will continue to co-fund meritorious, peer-reviewed HIV/AIDS projects through the HIV/AIDS Infrastructure Initiative of the Research Centers in Minority Institutions (RCMI) program.

Training

NIAID will continue supporting training efforts that encourage underrepresented minority investigators to pursue careers in biomedical research. Specific plans include the following:

- NIAID will continue to support the minority training programs administered through National Institute of General Medical Sciences.

- NIAID will continue to fund the AIDS projects conducted in the National Center for Research Resources' RCMI program.
- NIAID will continue to provide support for the Richard M. Asofsky Scholars in Research initiative. NIAID expects to exceed 2003 successes in future years.
- The Intramural NIAID Research Opportunities (INRO) program will be expanded to 5 days in 2004.
- NIAID continues to support the Enhancement Award for Underrepresented Minorities. The Enhancement Award initiative is expected to make several additional awards in FY 2004.
- NIAID will continue efforts to increase the number of minority researchers supported by RSUM. A Bridging the Career Gap seminar will be conducted in October 2005.
- NIAID will explore new concepts and ideas to improve outreach efforts to precollege students and will continue to support educational efforts at the middle and high school levels including the Temple Longitudinal Program, the Partners in Education Program, and Biomedical Research After School Scholars.
- NIAID will continue to actively recruit underrepresented minority researchers.

Outreach Activities

NIAID will continue its efforts to disseminate research results to the media, health professionals, and the public. Specific outreach activities include the following:

- NIAID will continue to implement innovative activities designed to improve awareness of biomedical research issues, awareness of clinical trials, and interest in biomedical research in underrepresented minority communities.
- NIAID will continue to support programs that increase the numbers of underrepresented minority individuals who pursue careers in biomedical research.
- NIAID will continue its efforts to increase public awareness of HIV vaccine and research and to recruit diverse volunteers for future clinical studies.
- NIAID will continue its outreach activities including producing and publicizing print, audiovisual, and Web-based materials; distributing materials at professional and community meetings; and sponsoring workshops and conferences for community health care providers and the public.
- NIAID will continue informing more than 400 voluntary and scientific organizations about Institute activities.



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