National Institute of Allergy and Infectious Diseases

PROFILE

Fiscal Year 2005

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

Front cover image: This is a representation of *Treponema pallidum*, the organism that causes syphilis.

National Institute of Allergy and Infectious Diseases

PROFILE

Fiscal Year 2005

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

National Institute of Allergy and Infectious Diseases

Published August 2006

National Institute of Allergy and Infectious Diseases

This is a stylized representation of an antibody, a protein made by the body's immune system cells to protect it against invading foreign substances.

INTRODUCTION

The National Institute of Allergy and Infectious Diseases (NIAID) conducts and supports basic and applied research to understand, treat, and prevent infectious and immune-mediated diseases. For more than 50 years, NIAID research has led to new therapies, vaccines, diagnostic tests, and other technologies that have improved the health of millions of people in the United States and around the world.

This *Profile*, which is published annually, describes the Institute's activities in basic research and clinical investigation and provides overviews of the major accomplishments and goals of the various scientific programs within the Institute. The *Profile* also includes information about the organization and staff of NIAID; the Institute's budget; and its extramural grants, contracts, and research training programs. Most importantly, it conveys the Institute's twofold mandate. First, NIAID must plan and execute a comprehensive and long-term basic and clinical research program on well-recognized endemic infectious and immune-mediated diseases. Second, it must respond quickly with targeted research to meet new and unexpected infectious disease threats as they arise, often in the form of public health emergencies. In this latter respect, NIAID is unique among the institutes of the National Institutes of Health (NIH). The scope of the NIAID research portfolio has expanded considerably in recent years in response to new challenges such as bioterrorism; emerging and re-emerging infectious diseases, including acquired immunodeficiency syndrome (AIDS), influenza, severe acute respiratory syndrome (SARS), West Nile virus, malaria, and tuberculosis; and the increase in asthma prevalence among children in this country.

Despite advances in medicine and public health such as antibiotics, vaccines, and improved sanitation, the World Health Organization estimates that infectious diseases still account for approximately 26 percent of all deaths worldwide, including about two-thirds of all deaths among children younger than 5 years of age. The pathogens are not static, but change dramatically as new microbes emerge and familiar ones re-emerge with new characteristics or in unusual settings.

Influenza is a classic example of a re-emerging disease. Influenza viruses continually accumulate small changes such that a slightly different vaccine must be made for each influenza season. When a new influenza virus against which people have no natural immunity emerges, a worldwide pandemic can result if the virus is able to transmit efficiently from person to person. In 2005, the accelerated spread among domesticated chickens of a virulent strain of H5N1 avian influenza that spread in a limited fashion from chicken to human spurred national and international public health professionals to prepare for the possibility of a global pandemic. For such a situation to develop, the H5N1 strain would need to acquire the ability to spread efficiently from animal to human and from human to human. On November 1, 2005, President George W. Bush announced the *National Strategy for Pandemic Influenza*. The *HHS Pandemic Influenza Preparedness and Response Plan,* an integral component of the *National Strategy,* designates NIAID as the lead agency for scientific research and clinical trials to foster product development, particularly vaccines and antiviral drugs, to prepare our nation for a potential human influenza pandemic.

Our ability to cope with an influenza pandemic will depend to a large extent on how well we cope with seasonal influenza, which each year kills an average of about 36,000 people in the United States alone. The serious vaccine shortage resulting from a manufacturing plant contamination that occurred in the 2004–2005 influenza season underscored the difficulties in annually renewing the influenza vaccine supply and highlights the need to move toward adoption

of newer vaccine manufacturing techniques and other strategies that can improve the surge capacity, flexibility, and speed with which vaccines are made. NIAID supports numerous research projects that lay the foundation for improved influenza vaccine manufacturing methods, new categories of vaccines that work against multiple influenza strains, and the next generation of anti-influenza drugs. NIAID also conducts surveillance for the molecular evolution of influenza viruses among animals and humans in Asia and elsewhere, and tracks changes in influenza viruses that might allow them to be transmitted more easily among people.

NIAID also focuses on other emerging and re-emerging infectious disease threats around the world. Malaria is a substantial and growing problem compounded by the emergence of drug-resistant malaria parasites and insecticide-resistant mosquito vectors. NIAID supports a large malaria research portfolio. One recent study in mice identified a specific parasite gene that is essential for full maturation of the parasites, a finding that could be useful in developing an effective malaria vaccine. NIAID also supports a large portfolio of research to develop new drugs, vaccines, and diagnostics for tuberculosis (TB), which is estimated to affect one-third of the world's population and is especially common among persons infected with HIV. Two novel, genetically engineered TB vaccines developed with NIAID support recently entered phase I clinical trials in the United States. These promising candidates are the first new TB vaccines to be tested in more than 60 years.

Vaccine research supported by NIAID has led to new or improved vaccines for a variety of serious diseases, including rabies, meningitis, whooping cough, hepatitis A and B, chickenpox, and pneumococcal pneumonia. With our partners in academia and industry, NIAID works to develop new vaccine candidates to prevent diseases for which no vaccines currently exist, improve the safety and efficacy of existing vaccines, and design novel vaccine approaches based on new vectors and adjuvants.

Despite recent progress in treatment and prevention, human immunodeficiency virus (HIV) disease and AIDS continue to exact an enormous toll throughout the world. An estimated 40 million people worldwide are living with HIV/AIDS, and their number is increasing by more than 5 million people every year—about 14,000 each day. More than 25 million people with HIV have died of HIV-related disease since the pandemic began.

To advance understanding, treatment, and prevention of HIV/AIDS, NIAID has established research collaborations with colleagues in more than 50 countries to develop comprehensive approaches to the HIV pandemic. These collaborations already have yielded important results, most notably in developing methods to reduce mother-to-child transmission of HIV. Development of a vaccine that protects against HIV/AIDS is one of the highest priorities of NIAID. To help overcome the extraordinary scientific challenges of HIV vaccine development, NIAID established the Center for HIV/AIDS Vaccine Immunology (CHAVI) in June 2005. CHAVI's mission is to tackle the fundamental immunological obstacles in HIV vaccine research and to design, develop, and test novel HIV vaccine candidates.

NIAID-supported researchers have made critical discoveries concerning the basic biology of HIV and the immune response to HIV infection, which in turn have led to the development of therapies that suppress the replication of the virus in the body. The use of potent combinations of anti-HIV drugs, many of which were developed with NIAID support, has dramatically reduced the numbers of AIDS deaths in industrialized countries and has saved the lives of hundreds of thousands of people in developing countries in sub-Saharan Africa, the Caribbean, South America, and Asia. Although much has been

learned in recent years, NIAID continues to investigate how the virus destroys the body's immune system and why the body fails to contain and eliminate the virus, both of which are critical for identifying additional targets for therapeutic interventions and vaccines.

The potential use of biological agents in a terrorist attack is a serious threat to the citizens of our nation and the world. Research to develop countermeasures against this threat is a key focus of NIAID. The *NIAID Strategic Plan for Biodefense Research,* developed shortly after the terrorist attacks of 2001, outlines three essential pillars of the NIAID biodefense research program: *infrastructure* needed to safely conduct research on dangerous pathogens; *basic research* on microbes and host immune defenses, which serves as the foundation for applied research; and targeted, milestone-driven development of *medical countermeasures* to create the vaccines, therapeutics, and diagnostics that would be needed in the event of a bioterror attack. In fiscal year (FY) 2003, NIAID was assigned the role of coordinating and facilitating NIH research into countermeasures to mitigate harm to civilians from chemical and radiological/nuclear weapons.

Two National Biocontainment Research Facilities as well as 13 Regional Biocontainment Laboratories, in which scientists will be able to safely contain and study dangerous pathogens, are now planned or under construction. NIAID also has established a nationwide network of 10 Regional Centers of Excellence (RCEs) for Biodefense and Emerging Infectious Diseases research. The investment in biodefense research already has yielded substantial dividends. NIAID basic research and clinical trials are greatly increasing our ability to respond to the threats of smallpox, anthrax, and Ebola with new and improved vaccines, and this work promises to yield new insights relevant to both common and newly emerging infectious diseases that afflict people in the United States and abroad. In particular, the advancement of knowledge about infectious organisms that could be used as weapons should also have an enormous positive impact on the ability to diagnose, treat, and prevent established major infectious diseases, such as malaria, tuberculosis, and HIV/AIDS, as well as emerging and re-emerging infectious diseases such as West Nile virus, dengue, influenza, and multidrug-resistant microbes. For example, in FY 2005, NIAID-supported scientists discovered that it might be possible to halt a poxvirus infection by administering a cancer drug aimed not at the virus but at the host cellular machinery that the virus needs to spread from cell to cell.[1] This research suggests a means of circumventing antiviral drug resistance for other viruses.

Another important NIAID research focus is the immune system, the complex network of cells, tissues, and organs that work together to defend the body against attacks by foreign invaders such as bacteria, viruses, parasites, and fungi. When the immune system attacks the wrong target, however, many diseases can result, including asthma and allergic diseases, rheumatoid arthritis, and other illnesses that cause significant, chronic disability in the United States and throughout the world. NIAID-supported research in basic and clinical immunology has led to many promising approaches for treating individuals with immune-mediated conditions such as multiple sclerosis, type 1 diabetes, and asthma. For example, researchers are developing novel ways to selectively block inappropriate or destructive immune responses while leaving protective immune responses intact, an area of research known as tolerance induction. NIAID has established the Immune Tolerance Network, a comprehensive program in which international researchers pursue research in immune tolerance induction. Currently, NIAID supports more than 40 clinical trials of immune tolerance strategies to treat autoimmune diseases, allergic diseases, and transplant rejection.

NIAID-supported research in immune-mediated diseases led to other significant advances in

FY 2005, such as a novel way to noninvasively assess the risk of kidney graft rejection by using immunologic and genetic biomarkers present in urine. If validated in larger studies, use of these biomarkers would allow physicians a noninvasive way to monitor transplant recipients for signs of organ rejection and to intervene before organ injury occurs. This would represent a significant advance in the clinical management of transplant patients.

NIAID also remains committed to improving the health of children with asthma, particularly those who live in our nation's inner cities. NIAID-supported researchers published the results of a study on the cost-effectiveness of home-based interventions that reduce exposure to common allergens such as cockroaches, house dust mites, and tobacco smoke. The study indicated that such interventions can result in 24 percent fewer unscheduled clinic visits, and a 13 percent reduction in the use of albuterol inhalers, small applicators that deliver asthma medication directly into the lungs. The reduction in symptoms persisted for at least 1 year after the intervention was stopped, showing that tailored interventions may have a substantial long-term impact on asthma symptoms and healthcare resource use among inner-city children. For example, unscheduled clinic visits were reduced by 24%. The reduction in symptoms persisted for at least one year after the intervention was stopped.[2]

Much remains to be discovered about many infectious and immune-mediated diseases and how best to diagnose, treat, and prevent them. However, with its strong array of basic, applied, and clinical studies, and talented investigators in the United States and abroad, NIAID will continue to develop innovative technologies and treatments to combat a wide range of important diseases that afflict humanity.

Anthony S. Fauci, M.D.
Director
National Institute of Allergy and Infectious Diseases

[1] Reeves PM et al. Disabling poxvirus pathogenesis by inhibition of Abl-family tyrosine kinases. *Nature Med.* 11(7):731-739 (2005).

[2] M Kattan *et al.* Cost-effectiveness of a home-based environmental intervention for inner-city children with asthma. *Journal of Allergy and Clinical Immunology* DOI:10.1016/j.jaci.2005.07.032.