American Thoracic Society

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In This Issue

Letter from the Editor

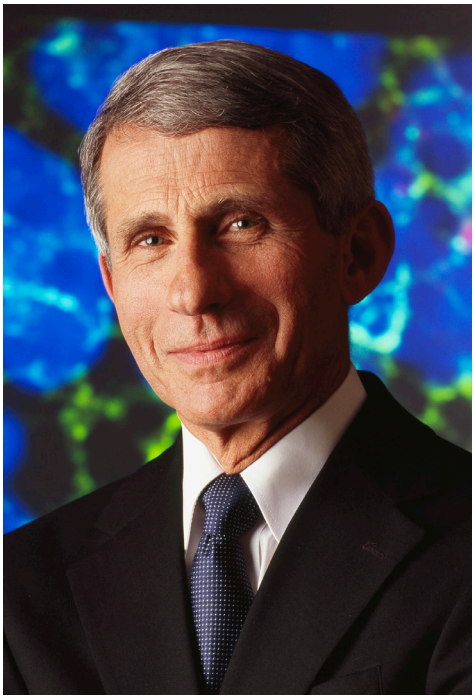
The October Research News Quarterly continues our interview series with National Institutes of Health and federal program heads with a conversation with the director of the National Institute of Allergy and Infectious Diseases, Anthony Fauci, MD. In this interview, Dr. Fauci outlines the institute's top priorities over the next five years in infectious diseases including HIV/AIDS, tuberculosis and influenza and the institute's leadership role in combating antibiotic resistance. He also reveals new initiatives in asthma and allergy and discusses the institute's efforts to develop a universal flu vaccine.

Next, we report on a recent ATS-NHLBI briefing for congressional staff on Capitol Hill featuring ATS leaders Marc Moss, M.D. and Polly Parsons, M.D., followed by a report on the NIH's proposed changes to human research protections, known as the Common Rule.

Moving to child health, we have an update on the NIH's new Environmental Influences on Child Health Outcomes program, then on to new NCATS-funded CTSA awards. The Research News Quarterly ends with our Washington Office report on 2016 health research funding.

Sincerely,

Linda Nici, MD
Editor



INTERVIEW WITH ANTHONY FAUCI, MD

National Institute of Allergy and Infectious Disease Director

Q: What is your vision for the institute over the next five years?

A: Every NIAID research and training effort directly supports our mission to conduct and support basic and applied research to understand, diagnose, prevent, treat, and ultimately, cure infectious and immune-mediated diseases. We advance this mission guided by a unique dual mandate: to maintain a robust portfolio of basic, translational, and clinical research in microbiology, infectious diseases, immunology and allergy to reduce the burden of endemic diseases that persist in populations, and also to respond rapidly to new diseases, or to those that change in their scope or virulence. In keeping with this mandate, NIAID will advance the following priorities for the next five years and beyond:

- NIAID is supporting research initiatives aimed at the goal of an "AIDS-free generation" in which new HIV infections, as well as illness and death due to AIDS, are rare. This goal is within reach, thanks to a sustained research effort over the 30-plus years since HIV was identified. We continue to refine and optimize HIV prevention modalities and therapeutics, and develop new ones to treat and prevent HIV infection. We also remain determined to develop a safe and effective HIV/AIDS vaccine—the holy grail of HIV research. Finally, we aspire ultimately to cure individuals with HIV—that is, to suppress the virus to the point where a person with HIV can suspend antiretroviral therapy without having the virus rebound.
- NIAID supports research to develop diagnostics, vaccines, and treatments for established infectious diseases, including malaria, diarrheal diseases, and respiratory diseases such as tuberculosis and influenza. In addition, our flexible research infrastructure ensures that we also can respond rapidly to emerging and re-emerging infectious disease threats, such as Ebola, chikungunya, and dengue. NIAID scientists and grantees are working toward platform technologies that can be applied to more than one disease so that we will no longer have to create new vaccines and treatments de novo as individual diseases emerge. Pandemic influenza is a looming threat, and development

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Anthony Fauci Interview *(Continued from page 2)*

of a universal influenza vaccine that generates long-lasting protection against multiple strains of seasonal and pandemic influenza is a top NIAID goal. Finally, microbes are increasingly resistant to drug treatments for many established and emerging infectious diseases, including multiple hospital-acquired infections, gonorrhea, and tuberculosis. Antimicrobial resistance is an urgent NIAID research priority.

- NIAID supports fundamental research to expand understanding of the regulation of the human immune system and improve treatment strategies for immune-mediated disorders such as asthma, allergy, autoimmune diseases, and transplant rejection. We are working to further delineate the mechanisms of immune function and how we might suppress aberrant mechanisms and enhance deficient ones.
- In today's global community, an infectious disease can have an impact halfway around the world if an insect or other vector, or an infected person, brings the pathogen to a new or distant locale. Infectious diseases are among the primary causes of mortality and suffering worldwide, and the reverberations of their impact can affect political and economic stability. NIAID embraces its leadership role in the global effort to defeat infectious diseases.

Q: The Administration is developing the historic National Action Plan for Combating Drug Resistant Tuberculosis. Among the key research action steps are the acceleration of efforts into the development of a new drug regimen to treat drug resistant TB. How is the institute implementing this action step in coordination with other government agencies, such as the U.S. Agency for International Development?

A: Growing concern about the emergence of TB strains resistant to antibiotic treatments prompted development of the "U.S. Government National Action Plan for Combating Multidrug-Resistant Tuberculosis," a companion document to President Obama's "National Action Plan for Combating Antibiotic-Resistant Bacteria." The TB action plan identifies critical actions the U.S. government will take over a three to five-year period to achieve specific targets in TB research efforts, including development of new drug regimens, especially for the growing problem of multidrug-resistant and extensively drug-resistant TB. NIH/NIAID, CDC, and USAID each have a unique, yet complementary, role in this effort and will continue to coordinate efforts—as they currently do as members of the Federal TB Task Force.

At NIAID, we are working to bring TB treatment into the 21st century. NIAID's broad TB research portfolio is advancing early and translational research on drug-resistant TB, with the goal of developing new treatment regimens and diagnostics. We recently expanded the Tuberculosis Research Units program, which focuses on TB latency and persistence in connection with active TB disease. Through our intramural program, NIAID is part of the Bill & Melinda Gates Foundation-supported TB Drug Accelerator (TBDA), a collaborative effort with eight pharmaceutical companies and seven research institutions to develop a new TB drug regimen. The TBDA aims to generate multiple, distinct TB drug candidates by overcoming traditional bottlenecks in TB drug discovery.

NIAID also is working to develop better diagnostic tools to identify patients who harbor TB bacteria, especially people who are asymptomatic. The NIAID-supported TB Clinical Diagnostic Research Consortium is evaluating several investigational diagnostic approaches and their effect on TB management in countries where the disease is endemic. By supporting a wide array of research strategies and forging collaborations with other federal agencies and organizations, NIAID is determined to help alleviate the public health burden of this deadly disease.

Q: NIAID is at the forefront of the White House's initiative on Combating Antibiotic-Resistant

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Anthony Fauci Interview *(Continued from page 3)*

Bacteria. With the increasing prevalence of deadly resistant gram-negative bacterial pneumonia infections in the U.S., what are the prospects for development of a new rapid diagnostic test to more quickly detect these infections?

A: Alarming rates of drug-resistant Gram-negative infections, such as *Klebsiella*, *Pseudomonas*, and *Acinetobacter*, pose dangerous risks to vulnerable patients, especially in hospitals, nursing homes and other healthcare settings. NIAID is tackling this serious problem in several ways. One focus is novel diagnostics for detecting gram-negative pathogens in blood or urine and determining which drugs might be effective against a particular infection.

In 2013, NIAID launched the Antibacterial Resistance Leadership Group, which has a clinical research agenda focused on developing and testing therapies for Gram-negative and Gram-positive bacteria, assessing antibacterial stewardship programs, and evaluating methods to rapidly identify bacterial pathogens and infections. These methods include tests to differentiate viral and bacterial respiratory tract infections and rapid tests to inform decisions about antibiotic treatment. The ARLG also has established the Web-Based Virtual Biorepository Catalogue to provide investigators with unique access to clinically well-characterized Gram-positive and Gram-negative bacteria for the development of diagnostic tests. Recently, NIAID also made nine awards to support the development of new diagnostics to rapidly detect antimicrobial-resistant bacteria, including those common in healthcare settings.

Q: Are there new NIAID initiatives in allergy and asthma coming down the pipeline?

A: NIAID recently created a new program and recompeted existing ones to enhance our understanding of asthma and allergic disease. The Asthma and Allergic Diseases Cooperative Research Centers, established in 1971 and reissued in 2015, will continue to support integrated basic and clinical research on the mechanisms underlying the onset and progression of asthma. This initiative will also support research on other immune-related disorders, including allergic and non-allergic rhinitis, chronic rhinosinusitis, atopic dermatitis, and food and drug allergy.

The Consortium for Food Allergy Research, reissued in 2014, focuses on immune-based and other strategies for preventing and treating conditions associated with food allergens, such as severe allergic reactions and food-induced anaphylaxis. The consortium conducts basic research studies, clinical trials, observational studies, and mechanistic studies to better understand and improve treatment strategies for food allergy. In collaboration with NHLBI, NIDDK, and NIAMS, NIAID is implementing the new Research on Eosinophil-Associated Disorders program to encourage research to determine the cellular and molecular mechanisms of eosinophil-associated disorders, which can affect the immune system, upper and lower airways, cardiovascular system, and other organs.

Q: Can you comment on goals to permanently eradicate pandemic flu and efforts to create a universal influenza vaccine that is of particular interest to the pulmonary and critical care medicine community?

A: Influenza A viruses infect a wide range of animal hosts, which serve as reservoirs from which novel influenza A viruses can be introduced into the human population. Consequently, it is unlikely that we will be able to fully eradicate this virus. Effective preparedness, however, can go a long way toward mitigating the global public health toll of influenza pandemics, as well as seasonal epidemics. Widespread vaccination against seasonal flu is essential to preparedness, but

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NIAID is focused on an even greater goal: to develop a universal influenza vaccine that eliminates the need to formulate a seasonal vaccine each year in response to circulating influenza strains. Achieving a universal flu vaccine is one of the highest research priorities of NIAID and of NIH.

With an increasing understanding of the structure and immunological characteristics of the influenza surface protein hemagglutinin (HA), NIAID researchers and grantees are moving closer to breakthroughs in the development of a universal flu vaccine. Unlike the highly variable head portion of the mushroom-shaped HA molecule, the stem portion of the molecule remains relatively constant among different influenza strains and thus makes for a better cross-protective immunologic target.

NIAID, in collaboration with the Biomedical Advanced Research and Development Authority and the CDC, is initiating a phase I trial to investigate the human immune response to HA stem-based universal flu vaccine candidates. In other promising research, scientists at the NIAID Vaccine Research Center developed an HA-ferritin nanoparticle vaccine that, in pre-clinical studies, elicited neutralizing antibodies to HA structures that are targets of universal influenza vaccines. VRC scientists also are conducting research on influenza nanoparticle vaccine platforms that may improve the potency, breadth, magnitude, and durability of influenza virus immunity. In addition, NIAID researchers are advancing a novel vaccination strategy consisting of a mixture of virus-like particles, or VLPs. Beyond the push for a universal flu vaccine, NIAID is committed to support for basic research on influenza biology, and establishment and maintenance of a robust product development pipeline for influenza vaccines, treatments, and diagnostics.

Q: What is the commitment strategy of NIAID in recruiting and retaining an outstanding biomedical workforce and funding investigator-initiated research grants? Will the payline for these grants improve in the near future?

A: NIAID is proud to sustain a remarkable cadre of productive, creative, and highly accomplished grantees and intramural scientists. To continue this support, we rely on two pillars: extramural funding mechanisms to attract strong applications to funding announcements, and a flexible financial plan that enables us to fund as many high-quality R01s as possible. NIAID uses a differential R01 payline for new investigators to improve their chances of receiving a grant, and we pay special attention to new investigator status when we make select pay decisions. These actions give new investigators a competitive edge that they need to succeed.

Maintaining a strong payline for investigator-initiated grants is necessary to support talented scientists and enable them to continue conducting important research. It is no secret that in recent years, budgetary constraints have not allowed us to make substantial improvements in the payline. Nonetheless, NIAID's overall success rates for investigator-initiated research project grants have remained high (21.5 percent in fiscal year 2014). Success rates for training grants, fellowships, and career development awards have been even higher—greater than 30 percent in most cases—compared to research project grants. We are pleased that recipients of these early career awards have a higher success rate for getting their first R01 compared to researchers who did not receive such training grants early in their careers. ■

ATS CONVENES CONGRESSIONAL BRIEFING WITH NHLBI ON CRITICAL CARE RESEARCH

In September, ATS Vice President Marc Moss, MD, and ATS Secretary-Treasurer Polly Parsons, MD, along with NHLBI Director Gary Gibbons, MD, and ARDS Foundation President Eileen Rubin, spoke at an educational briefing for congressional staff on Capitol Hill sponsored by the ATS, NHLBI, and ARDS Foundation. The briefing, "ARDS and Sepsis Research: How Science is Improving Outcomes for Critically Ill Patients," showcased research advances supported by NHLBI that have saved lives and improved long-term outcomes for patients with sepsis, ARDS, and other critical illnesses.

Dr. Gibbons gave an overview of the public health burden of sepsis and ARDS in the U.S. and NHLBI's main critical care studies. Ms. Rubin eloquently told her story of how ARDS changed her life and the enormous challenges that patients with this disease have to overcome. Drs. Moss and Parsons discussed ongoing research on biomarkers and new therapies for sepsis and ARDS, showing how these and other discoveries over the past few decades have reduced patient mortality. They emphasized, for policymakers and their staff, how these advances were made possible by NIH support. The briefing is part of an ongoing educational series on lung, critical care, and sleep research for members of Congress and staff that the ATS sponsors with the NHLBI, and patient organizations. ■

Gary Gibbons, MD, director, NHLBI; Eileen Rubin, president, ARDS Foundation; Polly Parsons, MD, secretary-treasurer, ATS; Marc Moss, MD, vice president, ATS.

HUMAN RESEARCH PROTECTIONS

NIH Proposes Rules to Modernize and Strengthen Human Research Protections

In September, the National Institutes of Health's Office of Human Research Protections released a proposed rule to modernize and strengthen the Common Rule governing human research protections. The Common Rule protections were established in 1991 when research studies were conducted mainly at single-site academic and medical institutions. The extension of research into multi-site studies, different scientific disciplines and more patient engagement, in addition to technology advances led NIH to begin a process to update the protections in 2011 in response to this changing research environment with an initial set of proposals for public review, which included updating patient informed consent procedures and single institutional review board (IRB) review for multi-site studies. The single site IRB review has been maintained in the new draft rule, with certain exceptions.

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HUMAN RESEARCH PROTECTIONS *(Continued from page 6)*

In order to encourage the use of IRBs that are otherwise not affiliated with or operated by an assurance-holding institution ("unaffiliated IRBs"), a new process for outlining how such IRBs would be held directly responsible for compliance with the Common Rule. The rules also propose to eliminate the continuing review requirement for studies that undergo expedited review and for studies that have completed study interventions and are merely analyzing data or involve only observational follow-up in conjunction with standard clinical care.

The proposals would significantly tighten the patient informed consent process to ensure that individuals have a clearer understanding of the scope of studies, including risks and benefits, as well as alternatives to participating in the study. The rules also attempt to strengthen the effectiveness and efficiency of the oversight system by making the level of review more proportional to the seriousness of the harm or danger to be avoided. Research that poses greater risk to subjects would receive more oversight and deliberation than less risky research to the extent that some studies currently covered under the Common Rule would be exempt from its requirements. A new process would allow studies to be determined to be exempt without requiring any administrative or IRB review. The proposed rules envision the availability of a Web-based tool, whereby some investigators would be able to determine whether their studies are exempt.

The rules also outline significant changes to the informed consent process for the use of biospecimens in secondary research. Informed consent would be required for the use of stored specimens, such as left over blood or urine samples, in secondary research even if the investigator is not being given information that would enable him or her to identify whose biospecimen it is. However, patient consent for future use of biospecimens in unspecified research studies could generally be obtained at the time of the original consent process through broad consent to the storage and eventual use of samples. Certain exempt and all non-exempt research would be required to provide privacy safeguards for biospecimens and identifiable private information. These changes to patient consent procedures will be important for the new Precision Medicine Initiative, which will engage a cohort of one million patients in research to develop individualized treatments based on patient genetic information. The updated consent procedures could allow investigators to utilize the initiative's data and biospecimen bank for more secondary research, without having to complete additional patient consent.

In another significant change, the rule would extend the scope of the Common Rule's informed consent procedures to cover all clinical trials, regardless of funding source, conducted at a U.S. institution that receives federal funding for non-exempt human subjects research. Recognizing the impact of this change, the rule states that this provision will not take effect until three years after the final rule is published.

The proposed rule is open for public comment until Dec. 7. The public comments will then be reviewed by the agency for several months. A final rule is expected to be published in 2016. The American Thoracic Society Research Advocacy Committee will be drafting comments on behalf of the Society but individual ATS members are encouraged to provide their own feedback. Click here for a summary, press release and the full proposed rule. ■

PEDIATRIC RESEARCH

NIH Awards New Child Health Grants

The NIH recently announced the awarding of $144 million in grants to develop new tools to measure, record and analyze environmental influences on child health and development. The projects, part of the new

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PEDIATRIC RESEARCH *(Continued from page 7)*

Environmental Influences on Child Health Outcomes program, are some of the child health initiatives replacing the now terminated National Children's Study. The studies will be funded jointly through the National Institute of Biomedical Imaging and Bioengineering, National Institute of Environmental Health Sciences, National Institute of Child Health and Development, National Center for Advancing Translational Sciences, and the National Institute of Arthritis and Musculoskeletal and Skin Diseases.

The first set of awards will be for the development of new tools to improve research on the environmental influences of pediatric disease. One project, the Pediatric Research Using Integrated Sensor Monitoring Systems (PRISMS) initiative, is aimed at developing sensor-based, integrated health monitoring systems to measure environmental, physiological and behavioral factors in epidemiological studies in children. A number of studies involving pediatric asthma are being funded, including: "A Wearable Monitor for Pediatric Asthma: Developing Environmental and Breath Sensors Linked to Spirometry" through the University of California, Davis. The Children's Health and Exposure Analysis Resource, which will provide all NIH investigators with access to laboratory and statistical analysis to facilitate the inclusion of environmental exposures in more research projects. Finally, this initiative will support the Pediatric Patient Reported Outcomes in Chronic Diseases Consortium, which will utilize recent advances in patient-outcomes reporting.

A second initiative will examine the influence of the environment on in utero development to identify the cause of future diseases and conditions and extend the Human Placenta Project to identify technology gaps and develop new technologies or new applications to study the efforts of environmental factors on placental structure and function throughout pregnancy. An additional project will supplement existing grants on later child development to add or enhance high-dimensional molecular analysis strategies in current pregnancy, birth, and children's environmental health populations.

RESEARCH ADVOCACY

Pennsylvania ATS Members Meet with Key House Representative

ATS Pennsylvania members from the Division of Pulmonary, Allergy and Critical Care Medicine at Pennsylvania State University at Hershey met with Rep. Charlie Dent (R-PA) in his Hershey office in September. The ATS Pennsylvania delegation had a very engaging discussion with the congressman on research across a wide range of lung diseases at Penn State including COPD, asthma, cystic fibrosis, flu, pulmonary fibrosis, and sleep disorders. The ATS Pennsylvania members also discussed the health effects of e-cigarettes, including potential addiction risks to children and adolescents, and called for more research in this area. Rep. Dent is a key member of the House Labor-Health and Human Services Appropriations subcommittee, which allocates House funding for the NIH and CDC.

Zissis Chroneos, MD; Randy Young, MD; Rep. Charlie Dent (R-PA); Herbert Reynolds, MD; Lauren Van Scoy, MD; and Gavin Graff, MD.

NCATS Awards 18 New CTSA Hubs

The National Center for Advancing Translational Sciences recently announced funding awards that will support 18 new Clinical and Translational Science Awards Programs. The CTSA Program is a national network of research institution hubs focused on strengthening clinical and translational research. The hubs collaborate locally, regionally, and nationally, building on human subject research, patient involvement, new translational methodologies, and training. There are now more than 50 CTSAs program hubs in 31 states and the District of Columbia. The new awarded institutions include:

- Boston University
- Georgetown-Howard Universities, Washington, D.C.
- Medical College of Wisconsin, Milwaukee
- Northwestern University, Chicago
- University of Alabama at Birmingham
- University of California at San Diego
- University of Cincinnati
- University of Texas Medical Branch at Galveston
- Wake Forest University Health Sciences, Winston-Salem, North Carolina

View the full list of NCATS-funded CTSAs.

RESEARCH FUNDING

Congress Passes 2016 Spending Measure Averting Government Shutdown

On Sept. 30, the House and Senate passed a fiscal 2016 short-term spending measure to fund government agencies until Dec. 11, 2015, averting a government shutdown just hours before the expiration of fiscal 2015. The measure, known as a continuing resolution, imposes a 0.2108 percent across-the-board cut on all programs (including NIH) in order to remain under the current tight budget sequestration spending caps.

Just days prior to passage of the CR, a government shutdown appeared imminent as House and Senate Conservatives remained opposed to passing a spending measure that did not include language defunding Planned Parenthood. House Speaker John Boehner's announced resignation last week, however, strengthened the House leadership's position, albeit temporarily, to pass the CR. But the date of the expiration of the measure, Dec. 11, sets the deadline for the next political battle between congressional Republicans, Democrats, and the president over federal spending levels and policy riders such as Planned Parenthood and the Affordable Care Act. Although the threat of a government shutdown has been lifted for October and November, it remains a serious possibility again in December.

With passage of the fiscal 2016 CR, congressional leaders and the president have also begun negotiating on a new overarching budget agreement for the next two fiscal years to lift the current restrictive sequestration funding caps and ease funding reductions for government agencies.