

DEPARTMENT OF HEALTH AND HUMAN SERVICES
NATIONAL INSTITUTES OF HEALTH

Burden of Chronic Disease

Witness appearing before the
Senate Subcommittee on Labor-HHS-Education Appropriations

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Mr. Chairman and Members of the Committee:

I am pleased to present the Fiscal Year (FY) 2008 President's budget request for the National Institute on Aging (NIA). The FY 2008 request provides \$1,047,148,000 for the NIA.

Thank you for this opportunity to provide testimony for today's hearing. I am Dr. Richard Hodes, Director of the National Institute on Aging (NIA). The NIA leads a broad scientific effort to understand the nature of aging and to extend the healthy, active years of life. I appreciate the opportunity to discuss the burden of chronic disease, a critical issue for our older citizens.

The face of aging in the United States is changing dramatically and rapidly, according to a recent U.S. Census Bureau report commissioned by the NIA. Today, older Americans are very different from their predecessors, living longer, having lower rates of disability, achieving higher levels of education, and less often living in poverty. The baby boomers, the first of whom celebrated their 60th birthdays in 2006, promise to further redefine what it means to grow older in America.

While many of our seniors are enjoying their later years in good health, a number of chronic conditions remain common among older Americans. For example, more than half of all Americans over age 65 show evidence of osteoarthritis in at least one joint.¹ Over half of Americans older than 50 have osteoporosis or low bone mass,² and cardiovascular disease, cancer, and diabetes remain common among older Americans. Through research, we are discovering new and better ways to diagnose, treat, and even prevent these and other diseases and conditions.

The NIA provides leadership in aging research, training, health information dissemination, and other programs relevant to aging and older people. The Institute's robust research portfolio covers all aspects of aging, from the basic cellular and molecular changes that occur as we age, to the prevention and treatment of common age-related conditions, to the behavioral and social aspects of growing older, including the demographic and economic implications of an aging society. In addition, the NIA is the lead Federal agency for research related to the critically important effort to prevent and treat Alzheimer's disease. Finally, our education and outreach programs provide vital information to older people across the Nation on a wide variety of topics, including living with chronic conditions, maintaining optimal health, and caregiving.

¹ See "Handout on Health: Osteoarthritis," National Institute of Arthritis and Musculoskeletal and Skin Diseases, July 2002.

² See "America's Bone Health: The State of Osteoporosis and Low Bone Mass in Our Nation," National Osteoporosis Foundation, February 2002.

ALZHEIMER'S DISEASE AND THE NEUROSCIENCE OF AGING

While it is true that our senior and elderly citizens are aging far better today than in previous decades, the specter of Alzheimer's disease (AD), one of the most devastating neurodegenerative diseases, is a source of enormous concern as we and our loved ones age because of its enormous impact on individuals, families, the health care system, and society as a whole. Approximately 4.5 million Americans are currently battling AD, with annual costs for the disease estimated to exceed \$100 billion.³ Moreover, the rapid aging of the American population threatens to increase this burden significantly in the coming decades. By 2050, the number of Americans with AD could rise to some 13.2 million, an almost three-fold increase.⁴

AD is a chronic condition that advances gradually but inexorably, from early, mild forgetfulness to a severe loss of mental function called dementia. Eventually, people with AD become dependent on others for every aspect of their care taking a tremendous toll on family members and other caregivers, often for several years. The NIA supports an extensive research program with the goal of facilitating early diagnosis of AD and developing more effective preventive strategies and therapeutic interventions. Moving forward in each of these areas requires the translation of findings from the laboratory through preclinical testing and into full-scale clinical trials. Recent advances have been made on several fronts.

Neuroimaging. The discovery of compounds such as Pittsburgh Compound B and, more recently, FDDNP that enable the visualization of AD's characteristic amyloid plaques and neurofibrillary tangles in the living brain – an impossibility until several years ago – will not only enable scientists to diagnose AD earlier, but may also help researchers and clinicians develop new treatments and monitor their effectiveness, as well as reduce the time and cost of clinical trials. Research in this area has been intense and productive, with the Alzheimer's Disease Neuroimaging Initiative (ADNI) continuing to be a major venue for facilitating neuroimaging research relevant to AD.

Genetics. Discovery of risk factor genes will help illuminate the underlying disease processes of AD, open up novel areas of research, and identify new targets for drug therapy. Researchers recently determined that variations in a gene known as SORL1 may be a risk factor for the development of late onset AD. This discovery provides a new genetic clue about the late onset forms of AD. Further research is needed to determine the role of SORL1 in AD pathogenesis.

Research is continuing in this important area through the AD Genetics Initiative, which to date has recruited nearly 1,000 families to establish a data base for studies of familial inheritance of AD. In addition, the NIA has established a national genetics data repository to facilitate access by qualified investigators to genotypic data for the study of

³ Data from the Alzheimer's Association. See also Ernst, RL; Hay, JW. "The U.S. Economic and Social Costs of Alzheimer's Disease Revisited." *American Journal of Public Health* 1994; 84(8): 1261 – 1264. This study cites figures based on 1991 data, which were updated in the journal's press release to 1994 figures.

⁴ Hebert, LE et al. "Alzheimer Disease in the U.S. Population: Prevalence Estimates Using the 2000 Census." *Archives of Neurology* August 2003; 60 (8): 1119 – 1122.

the genetics of late-onset AD. Investigators have already begun submitting data to this repository and requesting additional data for genetic studies.

Pre-Clinical and Translational Research. NIA plans to speed drug discovery and movement of promising new treatments and prevention strategies into clinical trials. The launch of a major new translational research effort to expand the range of novel compounds to be tested for their effect in preventing or slowing progression of cognitive decline, mild cognitive impairment, and AD, and to more quickly move research from the laboratory to clinical trials in humans, will further support our efforts in this regard.

Clinical Research. The NIA is currently supporting approximately 25 AD-related clinical trials. NIA plans to use the knowledge gained through basic and mechanistic studies to select the most promising imaging and biological markers, as well as improved clinical and neuropsychological evaluation methods, to design and perform less expensive, shorter, and more efficient drug trials. Recent progress in understanding the basic genetic and molecular processes of AD has provided new mechanism-based approaches to designing interventions. NIA-supported researchers are also studying simple lifestyle changes that may confer protective benefits on cognition. For example, in one recent study, increased vegetable consumption was found to be associated with reduced risk of cognitive decline in women. In another, certain mental exercises were found to help older individuals maintain their cognitive abilities; the benefits may last as long as five years.

HEALTHY AGING

Preservation of cognition in specific domains can be of particular importance to the safety and independence of aging adults. For example, NIA-supported researchers have provided the underlying research for and developed the Useful Field of View (UFOV) test to help predict the degree to which a person may safely perform activities such as driving. The measure is now a major component of assessments tested and about to be adopted by three state Departments of Motor Vehicles for use in screening older drivers. NIA-supported research will also provide the foundation for development of training to help older adults improve their visual attention and speed of processing based on UFOV testing, and for the translation of this training as part of driving safety programs for older adults.

In addition to testing ways to maintain cognitive function, NIA-supported investigators are actively seeking ways to maintain physical function into older age. For example, several studies suggest that physical exercise may prevent physical disability, including impaired mobility, in healthy and frail older adults. To develop definitive evidence regarding the effectiveness of such interventions, NIA and grantee researchers have designed the LIFE (Lifestyle Interventions and Independence in Elders) study, a clinical trial testing the effects of a physical activity program vs. a health education program among older Americans in preventing major disability. A successful pilot study (LIFE-P) completed in 2005 showed both feasibility and positive preliminary data, permitting design and consideration of this large-scale clinical trial.

A large body of research in animal models indicates that substantially reducing caloric intake while maintaining optimal nutrition results in significant increase in life span. The NIA-supported Comprehensive Assessment of Long-Term Effects of Reducing Intake of Energy (CALERIE) will help to determine if these beneficial effects extend to humans. Results from pilot studies demonstrated that overweight people who cut their calories by 25 percent for six months have reduced fasting insulin levels and core body temperature, two markers that have been associated with increased longevity in animal models, and that may be similarly associated with human longevity. A two-year study will begin in early January 2007 to determine whether healthy non-obese men and women ages 25-45 who reduce their caloric intake by 25 percent maintain these metabolic changes, and will measure other long-term effects of sustaining lowered caloric intake on factors related to aging changes and risks for age-related diseases.

Because an intensive regimen of restricted food intake may prove difficult for many people to follow over the long term, and may in fact have adverse consequences in some circumstances, investigators are also searching for compounds that mimic the effects of caloric restriction on the body. One compound currently under study is resveratrol, an activator of a family of enzymes called sirtuins, whose cell-protective activities are themselves the subject of intensive scientific inquiry. In a recent study, overweight, aged male mice given a high-fat diet supplemented with resveratrol had better health and survival than aged overweight mice who did not receive the compound. Resveratrol's safety and effectiveness to address aging and age- or obesity-related conditions in humans have not been demonstrated, and further research is needed on the short- and long-term effects of resveratrol in animals and humans.

The NIA Intervention Testing Program supports the testing of compounds with the potential to extend the lifespan and delay disease and dysfunction in a mouse model. Plans are to renew this promising initiative in FY 2007 for funding in FY 2008. In addition, NIA is continuing to search for genes and biological pathways that influence longevity and aging through the Longevity Associated Gene initiative, which to date has identified over one hundred new longevity-associated genes, along with many conserved biological processes and pathways that regulate longevity in a host of divergent species, including humans.

New research findings may one day translate into better ways to support the aging immune system. A new initiative on Membrane Associated Signaling Defects in Immune Cells with Aging seeks to shed light on the cellular processes that may lead to impaired immune function in older people. This research may ultimately lead to the development of interventions to bolster the immune system and reduce vulnerability to disease and disability in older people.

Thank you for the opportunity to provide my testimony to this Subcommittee and to describe these examples of research targeted at improving the health and quality of life of aging and older adults. I would be happy to answer any questions you may have.

Richard J. Hodes, M.D.

Director, National Institute on Aging

Richard J. Hodes, M.D., directs the research program of the National Institute on Aging (NIA) at the National Institutes of Health. A leading immunologist, Dr. Hodes was named Director of the NIA in 1993, to oversee studies of the basic, clinical, epidemiological and social aspects of aging.

Under Dr. Hodes's stewardship, the NIA budget has surpassed \$1 billion, reflecting increased public interest in aging as America and the world grow older. Dr. Hodes has devoted his tenure to the development of a strong, diverse, and balanced research program, focusing on the genetics and biology of aging, basic and clinical studies aimed at reducing disease and disability, including Alzheimer's disease and age-related cognitive change, and investigation of the behavioral and social aspects of aging. Ultimately, these efforts have one goal -- improving the health and quality of life for older people and their families.

In the past decade, the NIA has worked in new and innovative ways to conduct research and to translate research findings into practical interventions and public information. In Alzheimer's disease (AD), new initiatives to find genes involved in AD and to identify biomarkers are expected to considerably reduce the length and cost of clinical trials, thereby speeding up the testing of new therapies for AD. In studies of the basic biology of aging, research conducted and supported by the NIA examines the genetic and other factors influencing lifespan and age related diseases and conditions. Research in geriatrics and clinical gerontology is uncovering new ways to combat the development of frailty and disability with age, and social and demographic research is deepening understanding of the individual behaviors and societal decisions that affect well-being.

Dr. Hodes is a Diplomate of the American Board of Internal Medicine. In 1995, he was elected as a member of The Dana Alliance for Brain Initiatives; in 1997, he was elected as a Fellow of the American Association for the Advancement of Science; and in 1999, he was elected to membership in the Institute of Medicine of the National Academy of Sciences.

Dr. Hodes is a graduate of Yale University and received his M.D., from Harvard Medical School. As an author of more than 200 research papers, he is an influential scientist in and contributor to the field of immunology.

Department of Health and Human Services
Office of Budget
Richard J. Turman

Mr. Turman is the Deputy Assistant Secretary for Budget, HHS. He joined federal service as a Presidential Management Intern in 1987 at the Office of Management and Budget, where he worked as a Budget Examiner and later as a Branch Chief. He has worked as a Legislative Assistant in the Senate, as the Director of Federal Relations for an association of research universities, and as the Associate Director for Budget of the National Institutes of Health. He received a Bachelor's Degree from the University of California, Santa Cruz, and a Masters in Public Policy from the University of California, Berkeley