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Good afternoon. I am Dr. Richard Hodes, Director of the National Institute on Aging (NIA), one of the 27 Institutes and Centers of the U.S. National Institutes of Health and the lead federal agency for research on Alzheimer's disease (AD). It is a pleasure to be here today to discuss our work with partners around the world to understand, prevent, and treat AD.

Alzheimer's disease – the most common form of dementia – and related dementias represent a considerable global health burden. In the United States alone, as many as 5.1 million individuals may have AD.[1] Worldwide, an international team of researchers recently estimated that over 24 million people suffer from dementia, with approximately 4.6 million new cases every year; approximately 70 percent of these cases are likely AD. The number of people affected is expected to double every 20 years and will reach 81.1 million by 2040. Most people with dementia live in developing countries (60% in 2001, rising to 71% by 2040), and the projected increase in prevalence is expected to be particularly dramatic in low and middle income nations.[2] Among individuals ages 65 and older with dementia, experts estimate that just over half have AD, 16 percent have vascular dementia, and 30 percent have another form of dementia.[3]

As part of our comprehensive program of basic, clinical, and translational research on AD, NIH collaborates with a number of international partners to broaden understanding of the disease, to identify potential risk and protective factors, and to support the family members and others who care for patients with AD. We are also engaged in the broad coordination of research efforts around the world, including the exchange of cutting-edge information at influential global forums such as the International Conference on Alzheimer's Disease. In addition, NIA is a member of the Department of Health and Human Services Interagency Group on Alzheimer's Disease and Related Dementias, which was established this year to support the goals articulated in the National Alzheimer's Project Act (PL 111-175). This group is charged with "coordinat[ing] with international bodies to integrate and inform the fight against Alzheimer's

[1] Hebert LE, Scherr PA, Bienias JL et al. Alzheimer disease in the U.S. population: prevalence estimates using the 2000 census. Arch Neurol 60: 1119-1122, 2003.
[2] Ferri CP, Prince M, Brayne C et al. Global prevalence of dementia: a Delphi consensus study. Lancet 366: 2112-2117, 2005.
[3] Kester MI and Scheltens P. Dementia: The Bare Essentials. Pract Neurol 9: 241-251-, 2009.

globally." HHS has already begun reaching out to other countries to discuss the best way to carry out this coordination.

I'd like to focus on three critical areas today that have particular importance in the international context – understanding the roots of AD, seeking ways to better detect and diagnose it, and supporting for the caregivers that are the backbone of our care system for AD patients.

Understanding Alzheimer's Disease

Ongoing studies to elucidate the basic underpinnings of AD will suggest pathways for the development of preventive and treatment interventions. NIH has established the Dominantly Inherited Alzheimer's Network (DIAN), a consortium of scientific investigators from the United States, England, and Australia who will identify, recruit, evaluate, and follow up individuals from families with early onset dominantly inherited AD, a rare form of the disease. The scientists involved in this study hope to identify the sequence of brain changes in early-onset AD, before symptoms appear, and by understanding this process to also gain insight into the more common late-onset form of the disease.

Identification of genes that influence risk is an active and productive area of study. Until recently, only one gene variant, Apolipoprotein E-e4 (APOE-e4), had been confirmed as a significant risk factor gene for late-onset AD, the more common form of the disease. In the last several years, however, researchers have confirmed additional gene variants as possible risk factors for late-onset Alzheimer's, including SORL1, CR1, CLU, and PICALM – the latter two of which were identified in a study pooling DNA samples from a number of U.S. and European research groups. More recently, the NIH-supported Alzheimer's Disease Genetics Consortium (ADGC) coordinated a team of American, British, and Canadian researchers in a study that confirmed yet another gene variant, BIN1, and identified four others that may be risk factors.

Earlier this year, ADGC investigators joined with other research groups around the world to establish the International Genomics of Alzheimer's Project (IGAP), a global collaborative effort to identify additional genes that contribute to AD risk and influence progression of the

disease. IGAP researchers have created a shared resource database that includes genetic data for more than 40,000 individuals. This large, multinational data set will enable the researchers to identify rare genetic variants that would be impossible to find in smaller study populations, as well as find population-specific differences in genetic risk.

The identification of other risk and protective factors for cognitive impairment and dementia is a high priority for NIH. Ongoing studies are providing a wealth of information about the relationship between an array of economic, demographic, and lifestyle variables and cognitive health at the national and international levels. The long-running Health and Retirement Study (HRS), the U.S.'s leading source of combined data on health and financial circumstances of Americans over age 50, collects data on the cognitive health of older Americans, and similar surveys are ongoing in Europe, Mexico, Asia, and Africa. Efforts are currently underway to enhance cross-comparability of these surveys, which will facilitate innovative cross-national research. NIH also supports and encourages the inclusion of questions about cognitive health in other international data collection efforts, including surveys in Brazil, Ireland, and Japan.

These studies have already generated intriguing findings about interventions and lifestyle factors that may protect cognitive health. For example, NIH-supported investigators studying older populations in the U.S., England, and 11 European countries recently found that early retirement (prior to age 65) was associated with a significant decline in cognitive performance. The investigators suggest that this may be in part because for many people retirement leads to a less stimulating daily environment, and the prospect of retirement reduces the incentive to engage in mentally stimulating activities on the job. Although further study is needed, these findings suggest that the recent trend of American workers delaying retirement may eventually lead to improved cognitive performance in this group.

Another important effort is the Indianapolis-Ibadan Dementia Project compares the risk of dementia among community-dwelling African American elders in Indianapolis with the risk among their counterparts in the city of Ibadan, Nigeria. This study was one of the first to underscore the importance of vascular risk factors to AD pathogenesis. Further, a collaborative study between American and Israeli investigators is examining long-term characteristics of type

2 diabetes and inflammation and how they affect the development of cognitive decline among cognitively normal diabetic individuals 65 years and older living in Tel Aviv. A third project is exploring the possible association between exposure to certain trace elements and cognitive decline and dementia among elderly individuals in rural China.

Detection, Diagnosis, and Biomarker Identification

The NIH-supported Alzheimer's Disease Neuroimaging Initiative, a public-private partnership involving collaboration among government, academic, and industry partners, is the most comprehensive effort to date to find neuroimaging and other biomarkers for the progressive changes associated with AD and mild cognitive impairment (MCI is often a precursor condition to AD). ADNI investigators are testing whether serial imaging and other biomarkers and clinical and neuropsychological assessment can be combined to measure the progression of MCI and early AD. They made a significant step forward recently in developing an experimental test to diagnose the early stages of AD more accurately by measuring two biomarkers—tau and beta-amyloid proteins—in cerebrospinal fluid. These findings facilitated the first revision in 27 years of the clinical diagnostic criteria for AD, which characterize – for the first time – preclinical stages of the disease and address the use of imaging and fluid biomarkers to detect AD's onset and track its progression and (potentially) response to treatment.

An extension of the original ADNI, ADNI2, began last year. The overall goal is to determine the relationships among the clinical, cognitive, imaging, genetic and biochemical biomarker characteristics of the entire spectrum of AD, as the pathology evolves from normal aging through very mild symptoms, to MCI, to dementia. ADNI2 includes several Canadian sites which receive some funding from the Canadian Institute of Health Research.

Importantly, clinical, imaging, and biological data from ADNI are immediately made available to all qualified scientific investigators in public and private sectors worldwide, whether they are part of the study or not. Many of the tools and methods developed by the study have fueled similar efforts in Japan, the European Union, and Australia; Chinese, Korean, and Taiwanese versions of ADNI are also being established.

Helping Alzheimer's Caregivers

People with AD are frequently cared for in the home, and the physical and emotional toll AD exacts on family, caregivers, and friends can be significant. REACH II (Resources for Enhancing Alzheimer's Caregiver Health), an NIH-funded study, was the first intensive caregiver support intervention to be proven effective, through rigorous testing, in an ethnically diverse population. The REACH intervention is currently being translated more broadly through the U.S. Department of Veterans Affairs, which is now offering the program to veterans and their families and is beginning to test the intervention with caregivers of patients with other devastating chronic conditions. The Administration on Aging also is implementing the REACH intervention at centers in several states.

Recently, researchers at the University of Hong Kong have begun to adopt REACH through the Reaching Out Dementia Caregiver Support Program. This program, which is coordinated by the Hong Kong Council of Social Service, is the first international adaptation of the REACH intervention, and we are delighted to help foster this promising collaboration between Hong Kong and the American investigators involved in REACH.

Although geographic, language, and cultural differences exist within the international research community, we share an important goal: the reduction, and eventual elimination, of the devastation brought on by Alzheimer's disease. We look forward to continuing to work together with our international partners to reduce the burden of AD not just in the United States but throughout the world.

Thank you. I welcome your questions.