DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

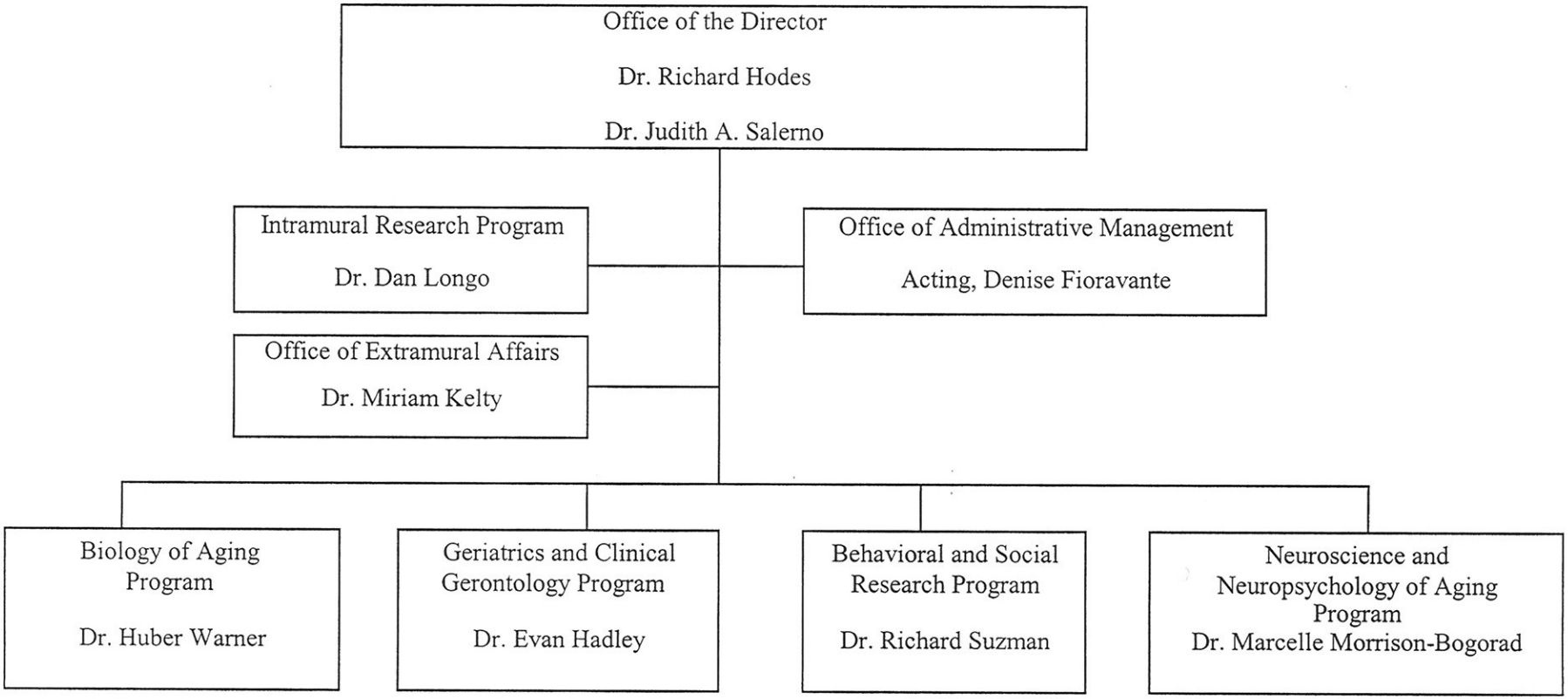
National Institute on Aging

FY 2006 Budget	Page No.
Organization chart	2
Appropriation language	3
Amounts available for obligation	4
Justification narrative	5
Budget mechanism table	26
Budget authority by activity	27
Summary of changes	28
Budget authority by object	30
Salaries and expenses	31
Significant items in House, Senate and Conference Appropriations Committee Reports	32
Authorizing legislation	43
Appropriations history	44
Detail of full-time equivalent employment (FTE)	45
Detail of positions	46

NATIONAL INSTITUTES OF HEALTH

National Institute on Aging

Organizational Structure



NATIONAL INSTITUTES OF HEALTH

National Institute on Aging

For carrying out Section 301 and title IV of the Public Health Service Act with respect to aging, [$1,060,666,000] *$1,057,203,000*.

[Department of Labor, Health and Human Services and Related Agencies Appropriations Act, as enacted by the Consolidated Appropriations Act for Fiscal Year 2005].

National Institutes of Health
National Institute on Aging

Amounts Available for Obligation 1/

Source of Funding	FY 2004 Actual	FY 2005 Appropriation	FY 2006 Estimate
Appropriation	$1,031,311,000	$1,060,666,000	$1,057,203,000
Enacted Rescissions	(6,557,000)	(8,676,000)	--
Subtotal, Adjusted Appropriation	1,024,754,000	1,051,990,000	1,057,203,000
Real transfer under NIH Director's one-percent transfer authority to other ICs	(3,373,000)	0	0
Comparative transfer to NIBIB for Radiology Program	(63,000)	0	0
Comparative transfer to Buildings and Facilities	(93,000)	0	0
Comparative transfer to/from other NIH ICs for NIH Roadmap	3,373,000	0	0
Subtotal, adjusted budget authority	1,024,598,000	1,051,990,000	1,057,203,000
Unobligated balance lapsing	(6,000)	0	0
Total obligations	1,024,592,000	1,051,990,000	1,057,203,000

1/ Excludes the following amounts for reimbursable activities carried out by this account:
FY 2004 - $2,054,000 ; FY 2005 - $4,400,000 FY 2006 - $4,400,000.
Excludes $830,000 in FY 2004 and $3,696,000 in FY 2005 for royalties.

Justification

National Institute on Aging

Authorizing Legislation: Section 301 of the Public Health Service Act, as amended. Reauthorizing legislation will be submitted.

Budget Authority:

FY 2004 Actual		FY 2005 Appropriation		FY 2006 Estimate		Increase or Decrease	
FTEs	BA	FTEs	BA	FTEs	BA	FTEs	BA
376	$1,024,598,000	379	$1,051,990,000	379	$1,057,203,000	0	$5,213,000

This document provides justification for the Fiscal Year 2006 activities of the National Institute on Aging (NIA), including HIV/AIDS activities. A detailed description of the NIH-wide Fiscal Year 2006 HIV/AIDS activities can be found in the NIH section entitled "Office of AIDS Research (OAR)."

INTRODUCTION

The mission of the NIA is to improve the health and well being of older Americans through an extensive program of high-quality research. There are currently 35 million Americans over the age of 65 – more than at any other time in history. Of these, more than four million are over 85, and some 65,000 have attained their hundredth birthday. In the coming years, the ranks of American elders are expected to swell; by 2030, the number of individuals age 65 and older likely will double, reaching 70.3 million and comprising a larger proportion of the entire population, rising from 13 to 20 percent.[1] In particular, explosive growth is anticipated among those most at risk for disease and disability, people age 85 and older, whose ranks are expected to grow from 4.3 million in 2000 to at least 19.4 million in 2050.

The aging of the population presents a number of social and economic challenges as increasing numbers of Americans reach retirement age. It also has important implications for our nation's health. For example, more than half of all Americans over age 65 show evidence of osteoarthritis in at least one joint.[2] Over half of Americans older than 50 have osteoporosis or low bone mass.[3] Cardiovascular disease, cancer, and diabetes remain common among older Americans, and as many as 4.5 million Americans suffer from Alzheimer's disease (AD).[4]

However, we now know that aging itself is not the cause of disease, disability, and frailty. Rather, disease and disabling processes influenced by age-related changes in the body and by unhealthy choices

[1] Federal Interagency Forum on Aging Related Statistics. *Older Americans 2000: Key Indicators of Well-Being.* 2000.
[2] See "Handout on Health: Osteoarthritis," National Institute of Arthritis and Musculoskeletal and Skin Diseases, July 2002.
[3] See America's Bone Health: The State of Osteoporosis and Low Bone Mass in Our Nation. National Osteoporosis Foundation, February 2002.
[4] Hebert LE et al.: Alzheimer disease in the U.S. population: Prevalence estimates using the 2000 Census. Arch. Neurol. 60: 1119-22, 2003.

and sedentary lifestyles are the most important factors in compromising the quality of life for older people. This fundamental shift in thinking was reinforced most recently with insights from the National Long Term Care Survey (NLTCS). According to this study, the rate of disability among older Americans dramatically declined from the 1980s through the mid 1990s, even among people age 85 and older. These findings, along with evidence from a number of other studies, suggest more strongly than ever that disease and disability can be delayed or even prevented through specific interventions.

At the same time, however, this downward trend in disability among the elderly is in real danger of reversal. Data from the National Health Interview Survey have found that, over the same period, the disability rate actually rose significantly for people ages 18-59, with the two most important causes of disability being musculoskeletal problems, particularly back problems, and mental illness. Findings also indicated that combined disability cases from musculoskeletal problems and diabetes, both of which can be associated with obesity, were increasing more rapidly by the mid-1990s than those from other problems, and that the growing prevalence of obesity is the dominant factor in the rise in disability among individuals ages 50-59.[5]

The NIA portfolio emphasizes research aimed at increasing the "healthspan,"or years of healthy, active life expectancy. With guidance from the National Advisory Council on Aging, the NIA conducts and supports research on the biochemical, genetic, and physiological mechanisms of aging in humans and animal models; the structure and function of the aging nervous system; social and behavioral aspects of aging processes and the place of older people in society; and the pathophysiology, diagnosis, treatment, and prevention of age-related diseases, degenerative conditions, and disabilities. In all of its efforts, the Institute pays special attention to reducing health disparities among different groups of Americans. NIA-supported researchers can be found in all fifty states, and the Institute also conducts a thriving program of training opportunities for researchers wishing to become involved in aging research.

NIA and the NIH Roadmap

Through a series of broadly based but well-integrated initiatives that address the need to advance our understanding of the complexity of biological systems; to explore new organizational models for team science; and to conduct even more efficiently the complex clinical studies needed to make rapid medical progress, the ultimate goal of the NIH Roadmap for Medical Research is to accelerate medical discovery and improve people's health. A number of the NIH Roadmap initiatives are particularly relevant to aging research. For example, the "Molecular Libraries and Imaging" component of the Roadmap will offer biomedical researchers access to small molecules that can be used as chemical probes - providing new ways to explore the functions of genes, cells, and biochemical pathways in healthy aging and disease. Small molecule development, by providing chemical compounds to validate new drug targets, is crucial to the development of drugs for a variety of age-related diseases, degenerative conditions, and disabilities. The refinement of molecular imaging techniques, particularly those for imaging brain function, can similarly be accelerated by enhancing the development and availability of small molecule libraries, and could, in turn, greatly enhance our ability to diagnose and monitor neurological conditions such as Alzheimer's disease.

---

[5] Lakdawalla DN, Bhattacharya J, Goldman DP. Are the Young Becoming More Disabled? Health Affairs 23(1): 168-76, 2004.

Another major theme of the NIH Roadmap is "Re-engineering the Clinical Research Enterprise." Clinical trials are necessary to the development of new treatments for age-related conditions, but many aspects of patients' subjective experiences - such as symptom severity and frequency, emotional and social well-being, and perceived level of health and functional ability - are not adequately captured by conventional clinical and functional measures of disease status, even though they are important targets for treatment interventions. Correctly measuring patient-reported outcomes can be particularly challenging with regard to the ways in which chronic diseases and their treatments affect the elderly. One Roadmap initiative has established a network of investigators to improve the measurement of patient-reported outcomes from a diverse population of individuals, having a variety of chronic diseases. Ongoing projects of particular relevance to the aged population are addressing pain, fatigue, arthritis, psychiatric symptoms, including depression, and social functioning.

ALZHEIMER'S DISEASE AND THE NEUROSCIENCE OF AGING

Alzheimer's disease (AD) is the most common cause of dementia among people age 65 and older, and is a major public health issue for the United States because of its enormous impact on individuals, families, the health care system, and society as a whole. Scientists now estimate that as many as 4.5 million people currently suffer with the disease, and this number is expected to increase to 13.2 million persons by 2050, an almost three-fold increase.[6]

People with AD gradually suffer memory loss and a decline in thinking abilities, as well as major personality changes. These losses in cognitive function are accompanied by pathologic changes in the brain, including the buildup of insoluble protein deposits called amyloid plaques and the development of neurofibrillary tangles, which are abnormal collections of twisted protein threads found inside nerve cells. Such changes result in death of brain cells and breakdown of the connections between them. AD 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. A diagnosis of AD is also associated with a sharply reduced lifespan; for example, the overall median survival for 70-year-olds in the United States is 15.7 years for women and 12.4 years for men, but a recent study found that this drops to 8.0 years and 4.4 years, respectively, for women and men with AD.[7]

The Genetics of Alzheimer's Disease

To date, only four of the approximately 30,000 genes in the human genome have been conclusively shown to affect the development of AD pathology. Three genes, amyloid precursor protein (APP), presenilin (PS) 1, and PS 2, are linked to the early-onset form of familial AD, which accounts for only a small percentage of all AD cases. A form of a fourth gene, APOE-ϵ4, which occurs in about one-fourth of the population, is a risk factor gene for late-onset AD (LOAD), and about half the AD cases have the ϵ4 form of the APOE gene. Geneticists have suggested that as many as four additional and as yet unidentified genes, at least one of which may be located on a specific region of chromosome 10, may be risk factor genes for LOAD. Finding new risk factor genes will help to identify pathways affecting the development or progression of AD, which can be become potential targets for treatment interventions.

---

[6] Hebert, op.cit.

[7] Larson EB, Shadlen MF, Wang L, McCormick WC, Bowen JD, Teri L, and Kukull WA: Survival after initial diagnosis of Alzheimer disease. Ann Intern Med 140: 501-509, 2004.

Changes in gene activity in early aging and Alzheimer's disease. Analysis of gene activity in discrete brain regions can provide important insights into the activities that underlie both normal brain aging and the pathological processes of neurodegeneration. Two recent studies demonstrate the utility of this approach. In one, investigators concluded that accelerated DNA damage may contribute to reduced gene expression, particularly the activity of genes involved in learning, memory and neuronal survival, and initiate a program of brain aging that starts early in adult life – in this case, around age 40. In a separate study, researchers show widespread changes in the genomic regulation of multiple pathways that involve the overactivity of tumor suppressor genes, as well as in genes involved in the differentiation of cells associated with myelinated axons. This suggests a provocative, but plausible, new model of AD pathogenesis that could account for the characteristic progression of AD throughout the brain along myelinated axons.

Genetic variations among individuals influence the severity of Alzheimer's disease. Insulin degrading enzyme (IDE) degrades amyloid β, a major component of amyloid plaques. In a recent study, the stretch of genetic material on chromosome 10 that contains the IDE gene and two other nearby genes was assessed for changes at a single point in the genetic code - known as a single nucleotide polymorphisms or SNP - and for haplotypes, which are stretches of DNA inherited in common among groups of people, in AD and control samples. Quantitative measures that are important to AD diagnosis and severity were also clinically assessed. Data strongly indicated the presence of alleles (alternative forms of a gene) and haplotypes that confer risk for AD within this region, and suggested that genetic variation within or extremely close to the IDE gene impacts both disease risk and traits related to the severity of the disease. Implementation of this approach on a broader scale is likely to be an effective tool in genetic analysis of complex diseases.

Early Diagnosis of AD

Early diagnosis of AD would be beneficial. For patients and their families, a definitive early diagnosis provides the opportunity to plan and pursue options for treatment and care, while the patient can take an active role in decision-making. For clinicians, accurate early diagnosis facilitates the selection of appropriate treatments, particularly as new interventions are developed. For researchers, earlier and more accurate diagnosis facilitates clinical studies of new therapies and preventive measures by allowing early and more targeted intervention, before cognitive loss becomes significant. Research suggests that the earliest AD pathology begins to develop in the brain long before clinical symptoms yield a diagnosis, and scientists are searching for reliable, valid, and easily attainable biological markers that, along with genetic, clinical, and neuropsychological assessments, could identify cases very early in the course of disease.

Abnormal PET scans in young adults at genetic risk for Alzheimer's disease. Using positron emission tomography (PET), patients with AD typically show decreased glucose metabolism, which correlates with brain activity, in specific brain regions. Other studies have shown decreases in metabolism in these same brain regions in non-symptomatic middle-aged people who are at risk for AD. In a recent study, investigators extended these findings to show that cognitively normal people who are APOE ϵ4 carriers show the characteristic decreases in brain metabolism while in their 20s and 30s - decades before the possible onset of symptoms, and considerably earlier than previously recognized. These findings provide direct evidence that pathologic changes in the brains of APOE ϵ4 carriers can be seen many years before the onset of detectable cognitive decline and are consistent with the idea that AD

may develop over decades. Many experts believe that the degeneration leading to AD should be treated as early in the course of the disease as possible, so as promising drug treatments develop, it will be even more important to identify those at risk and make early diagnoses.

Imaging amyloid in the living brain. Until recently, there have been no imaging techniques that could effectively visualize characteristic AD pathologic features in the living human brain. However, investigators have developed a compound, Pittsburgh Compound B (PIB), that binds to brain amyloid and enables it to be imaged using PET. Another compound currently under development, IMPY, has shown promise in imaging amyloid plaques using single photon emission computerized tomography (SPECT) in a mouse model of AD. Although further research is needed, PIB, IMPY, and related compounds may ultimately play an important role in AD diagnosis, as well as studies of the pathology and course of the disease and evaluation of drug therapies targeted against amyloid deposits.

Changes in cognitive performance over time in people at risk for AD. Scientists tested cognitively intact individuals, ages 48-77, on several components of memory over a two year period. APOE $\epsilon 4$ carriers 60 and older showed a significantly greater decline over time in new learning of a list of words, as compared with noncarriers. No difference in verbal learning ability was seen between carriers and noncarriers younger than 60 years old. These results suggest that longitudinal assessment of new learning may be a sensitive measure for detecting early cognitive changes in pre-symptomatic people who are at risk for AD.

Preventing Alzheimer's disease

No intervention has been proven to prevent AD or even delay its onset, but scientists continue to seek risk and preventative factors for the disease, as interventions that impact the effect of a risk or preventative factor could potentially delay the onset of the disease or prevent it altogether.

Diabetes and decline in cognitive function. Diabetes mellitus (DM) affects about one in five persons over age 60 years,[8] and it has been associated with a variety of adverse health effects. Recently four large-scale studies - the Religious Orders Study (ROS), the Nurses' Health Study (NHS), the Multiple Outcomes of Raloxifene Evaluation (MORE) Trial, and the Rancho Bernardo Study (RBS) - linked DM to changes in cognitive function. The studies suggested the following: women with DM have an increased risk of developing substantial cognitive decline (NHS, MORE Trial, RBS); post-menopausal women whose blood glucose levels are elevated, but not yet in the "diabetic" range, i.e., "pre-diabetic," are also at risk for significant cognitive impairment (MORE Trial); and oral hypoglycemic agents may ameliorate the increased risk in women (NHS, RBS). One study (ROS) suggested that men and women with DM have an increased risk of developing AD, and that, for both sexes, DM affects different cognitive systems differently. Together, these results indicate that a successful public-health prevention strategy for DM may also have major consequences for preventing or delaying AD. They further suggest that patients with DM who receive treatment for their condition may receive some protection from cognitive decline, in addition to the therapeutic benefit for DM.

Abnormalities in lipid metabolism in nerve cells linked to AD. The pathogenesis of AD is tightly linked to amyloid beta ($A\beta$) deposition and oxidative stress, the cellular damage caused by free radicals,

[8] See http://diabetes.niddk.nih.gov/dm/pubs/statistics/index.htm. Statistics are taken from the 1999-2001 National Health Interview Survey and 1999-2000 National Health and Nutrition Examination Survey (estimates projected to year 2002).

which are byproducts of normal cellular metabolism. However, it remains unclear how these factors result in dysfunction and death of brain cells. In a recent study, NIH researchers measured amounts of different lipids in brain cells from AD and control patients and found that AD patients had much higher levels of cholesterol and a lipid called ceramide specifically in brain regions important for learning and memory. These increases were associated with increased damage to nerve cells caused by free radicals. When cultured nerve cells were exposed to Aβ, similar overproduction of cholesterol and ceramide occurred. The increases were prevented and the nerve cells were protected when they were treated with the antioxidant vitamin E or a drug that prevents the accumulation of ceramide. These findings suggest a model of AD development that involves the disturbance of ceramide and cholesterol metabolism. This research further suggests that diets and drugs that target lipid abnormalities may be beneficial in the prevention and treatment of AD. Such drugs include cholesterol-lowering drugs, or statins, and earlier epidemiologic studies have shown a strong association between the use of statins and lower rates of AD. In January 2003, the NIA initiated the Cholesterol Lowering Agent to Slow Progression of AD (CLASP) study, a clinical trial to investigate the safety and effectiveness of the cholesterol-lowering drug simvastatin to slow the progression of mild to moderate AD. It is expected to be completed in November 2006.

Treating AD and Cognitive Impairment

To date, the Food and Drug Administration (FDA) has approved four medications for the treatment of mild to moderate AD symptoms. The first, tacrine (Cognex®), has been replaced by three newer drugs – donepezil (Aricept®), rivastigmine (Exelon®), and galantamine (Reminyl®). In 2003, the FDA approved memantine (Namenda™), the first drug to treat moderate to severe AD. These drugs improve some patients' ability to carry out activities of daily living, help with behavioral symptoms, such as delusions and agitation, and can also maintain thinking, memory, and speaking skills for a period of time. However, none of these drugs can stop or reverse the disease process, and they appear to help only some patients and only for a period of months to a few years. Finding a truly effective intervention will depend on research progressing on a number of fronts, both in model systems and humans, and a major clinical research focus lies in testing the effectiveness of therapies in people without symptoms or who have only slight memory problems.

Vaccine that removes plaques may also remove tangles. One way to treat AD successfully may be to interfere with early pathological changes in the brain, including the development of amyloid-β deposits (plaques) and the formation of tau-based neurofibrillary tangles, which are the hallmark pathological lesions of AD. Previous research has shown that in mice, immunization against Aβ can result in removal of amyloid plaques and maintenance of cognitive function. Now, researchers have found that a vaccine designed to clear amyloid plaques may also be effective against tau-based neurofibrillary tangles. Investigators injected "triple transgenic" mice, in which plaques, tangles, and AD-like brain damage are all present, with an antibody to Aβ. They found that Aβ was removed from both around and – unexpectedly – within neural cells. More surprisingly, they found that the antibody also removed early-stage accumulations of tau, though not late-stage tau lesions that resemble human neurofibrillary tangles. The reduction of tau pathology following an anti-Aβ treatment suggests a direct link between these two hallmarks of AD, and indicates that targeting the removal of Aβ early in the disease course might also eliminate tau pathology - thus removing or reducing both cardinal features of AD.

Donepezil May Have Short-Term Benefit for Mild Cognitive Impairment. The first NIH AD prevention trial, comparing the effects of vitamin E, donepezil (Aricept®), or placebo in preventing AD in people diagnosed with mild cognitive impairment (MCI), recently concluded at more than 70 sites across the U.S. The study is part of the Alzheimer's Disease Cooperative Study (ADCS) clinical trials consortium supported by NIA. Preliminary data from this study indicated that people with MCI taking donepezil, but not Vitamin E, were at reduced risk of progressing to AD for the first 18 months of the 3-year study when compared with their counterparts on placebo. The reduced risk of progressing from MCI to a diagnosis of AD among participants on donepezil disappeared after 18 months, and by the end of the 3-year period, the probability of progressing to AD was the same as that for the Vitamin E and placebo groups. However, among the subjects who did develop AD, those in the donepezil group experienced a statistically significant delay of almost 6-months in the development of AD compared to the placebo group.

Raloxifene may reduce risk of cognitive impairment in postmenopausal women. Studies of hormonal influences on cognitive aging in women have reported conflicting results, with some studies demonstrating a decreased risk for AD among users of hormone therapy and others, notably the Women's Health Initiative Memory Study (WHIMS), showing that post-menopausal women on certain regimens were actually at higher risk for cognitive decline. In a recent study - the Multiple Outcomes of Raloxifene Evaluation (MORE) trial - the selective estrogen receptor modulator (SERM) raloxifene (Evista®), frequently prescribed for the prevention and treatment of osteoporosis, appeared to reduce the risk of cognitive impairment in postmenopausal women. SERMs are compounds that mimic estrogen's actions in some tissues, but block the action of the body's naturally occurring estrogen in others. Raloxifene, like estrogen, promotes bone growth; however, it has anti-estrogenic actions on the breast and uterus that reduce possible cancer-causing stimulation of these tissues post-menopause. Over 5000 MORE participants were assigned to either 60 mg/day of raloxifene, or 120 mg/day of raloxifene, or placebo, and their cognitive function was assessed over the three years of the study. The researchers found that women taking 120 mg/day had a 33 percent lower risk of developing mild cognitive impairment (MCI), frequently a precursor condition to AD, than the other participants. They may also have a reduced risk of developing AD or other dementia, although this finding was not statistically significant. Risk of cognitive impairment did not differ between the 60 mg/day and placebo groups. Although extremely preliminary, these results suggest that treatment with raloxifene may offer women cognitive benefits, with fewer health risks than traditional hormone therapy.

People with early AD can still learn. In a recent study of cognitive rehabilitation among AD patients, who were taking medications to slow disease progression, subjects were randomly assigned to either a "cognitive rehabilitation" (CR) group or a control "mental stimulation" (MS) group. The subjects in the CR group participated in a series of bi-weekly sessions in which they were taught practical strategies for enhancing their ability to perform routine tasks such as face-name recognition, making change, and balancing a checkbook. The subjects in the MS group participated in activities that required memory, concentration, and problem-solving skills. At the end of the study, those in the CR group showed significantly improved ability to associate faces and names, had faster mental processing speeds, were better oriented to time and place, and were better able to make correct change for purchases than those in the MS group, although neither group showed memory improvement for manipulating objects or balancing a checkbook. The improvements were still evident three months after the intervention ended. These findings suggest that by combining specific cognitive rehabilitation strategies, people with AD

can be helped to remain engaged in daily activities and retain a connection to their family and friends and the world as a whole for a longer period of time.

Exercise plus behavioral management improves physical function and mental health in AD patients. Research has shown that even the oldest adults can improve cardiovascular functioning and increase flexibility, balance, and strength with systematic exercise training. However, it is unknown whether an exercise program would help reduce functional dependence and delay institutionalization among patients with AD. In a recent clinical trial, AD patients received either routine medical care or participated in an exercise plus behavioral management program. The exercise program consisted of aerobic/endurance activities, strength training, balance, and flexibility training. At three months, outcomes in the patients in the intervention group improved while routine care patients declined, and these differences remained up to two years later.

Caregiving of AD Patients

Most of the over four million Americans with AD today are cared for outside the institutional setting by an adult child or in-law, a spouse, another relative, or a friend. Caregivers frequently experience significant emotional stress, physical strain, and financial burdens, yet they often do not receive adequate support. Several recent studies have explored the problems faced by caregivers of AD patients, as well as possible interventions to reduce their burdens.

Sustained benefit of supportive intervention for depressive symptoms in caregivers of AD patients. Family caregivers of relatives with Alzheimer's disease are at high risk for psychological distress, particularly clinical depression. This risk persists over the many years of caregiving and even after caregiving ends with the death of the care recipient. Investigators followed 406 participants in the NYU Spouse-Caregiver Intervention Study, a long-running study of an intervention for family caregivers of people with AD. Half of the spouse-caregivers received an initial period of intensive counseling, attended weekly support groups, and were encouraged on an ongoing basis to contact counselors for support. The second group of spouses was assigned to receive the "usual" support services for families of AD patients at the Center, which included information about resources and advice upon request, but no formal counseling.

When they began the study, the two groups showed comparable levels of depressive symptoms, but after one year, 29.8 percent of caregivers in the enhanced treatment group had symptoms of clinical depression compared with 45.1 percent of those in the usual care group. Significant differences between the two groups were found through the third year of follow-up. These results offer evidence that distress and depressive symptoms in family caregivers can be effectively eased and that the benefits can be sustained over a long period of time.

Long-term care placement of dementia patients and caregiver health and well-being. In a recent study of the transition experience caregivers undergo when institutionalizing a relative, investigators found that race/ethnicity, caregiver burden, and global cognitive function of the patient were important predictors of institutionalization. They also found that caregivers who reported that providing help to their relative made them feel more useful, needed, appreciated, and important were less likely to institutionalize the patient. After the patient was institutionalized, half of spouse caregivers and one-quarter of nonspouse caregivers reported visiting the care recipient at least once a day, and nearly all

reported visiting at least once a week. Spouses reported higher levels of depression both before and after placement and more anxiety after placement than non-spouse caregivers. These findings suggest that although caregiver bereavement studies have shown that caregivers demonstrate recovery in response to the death of their loved one, there appears to be less benefit to the caregiver from institutionalizing the relative, possibly because the caregiving role is not wholly relinquished after institutionalization.

Initiatives: AD and the Neuroscience of Aging

Advances in neuroimaging have the potential to transform the way we predict, diagnose, monitor, and even treat mild cognitive impairment and AD. The NIA is currently developing an Alzheimer's Disease Neuroimaging Initiative, a longitudinal, prospective, natural history study of normal aging, mild cognitive impairment, and early AD to evaluate neuroimaging techniques (e.g. MRI, PET) and other potential biomarkers of the disease. Biomarkers may decrease the time and cost of clinical trials, which would increase the safety and efficiency of drug development. An important aspect of this initiative is that the clinical, imaging, and biological data and samples will be made available promptly to all qualified scientific investigators in academic as well as industrial research communities. The initiative is planned as a partnership among the NIA/NIH and several other private and government organizations.

The NIA is accelerating the pace of Alzheimer's disease genetics research with its AD Genetics Initiative, a major new program to speed the process of creating a large repository of DNA and cell lines from families with multiple AD cases. The goal of this initiative is to develop the resources necessary for identifying the remaining late-onset AD (LOAD) risk factor genes, associated environmental factors, and the interactions of genes and the environment. The AD Genetics Initiative will intensify sample collection and encourage data sharing by providing access to the repository to qualified investigators.

REDUCING DISEASE AND DISABILITY

About 79 percent of people age 70 and older have at least one of these seven potentially disabling chronic conditions - arthritis, hypertension, heart disease, diabetes, respiratory diseases, stroke, and cancer.[9] Other chronic conditions can compromise the health and quality of life of older Americans, as well; for example, a recent study found that 11 percent of U.S. men and 10.2 percent of U.S. women over age 65, and fully 20 percent of Americans over age 85, have anemia. This condition, while usually treatable, is often under-diagnosed and can be associated with a number of adverse health outcomes.[10] The burden of such chronic conditions is felt not only by individuals, but also by families, employers, and the health care system. Research to improve understanding of the risk and protective factors for chronic disease and disability can lead to the development of effective prevention strategies.

Treatment and Prevention of Disease

An asthma drug improves heart function and prevents further damage in rats with heart disease. The β-adrenoreceptors (β-ARs) receive and react to nerve impulses in certain tissues throughout the body. In the heart, there are at least three types of β-AR, each found primarily in a different type of cardiac tissue and each causing different effects when activated. Suppression of β_1-adrenoreceptors

[9] National Center for Health Statistics. *Health, United States, 1999 with Health and Aging Chartbook.* Figure 11, pg. 41. Hyattsville, MD: 1999.
[10] Guralnik JM, Eisenstaedt RS, Ferrucci L, Klein HG, and Woodman RC. Prevalence of anemia in persons 65 years and older in the United States: Evidence for a high rate of unexplained anemia. Blood 104: 2263-2268, 2004.

through the use of "beta blockers" is a standard treatment for congestive heart failure, which currently affects around five million Americans,[11] while drugs that stimulate β_2-ARs act as vasodilators and are commonly used in asthma inhalers. In addition, laboratory studies have shown that continuous stimulation of β_2-ARs protects heart cells from premature death.

NIH researchers have achieved promising results using a β_2-AR stimulator in a rat model of heart disease. After inducing heart attacks in rats, they treated one group with a beta blocker, metaprolol, while additional groups received continuous treatment with one of two β_2-AR stimulators, either fenoterol or zinterol. A final (control) group received no treatment. After six weeks, the rats' heart function was assessed and heart tissue was examined. The researchers found that the β_2-AR stimulators were more effective than metaprolol in preventing further cell damage and death. In addition, treatment with fenoterol or zinterol, unlike metaprolol, was actually associated with improved heart function in the diseased rats. These results suggest that β_2-AR stimulators, already widely in use for the treatment of pulmonary disease, may also be effective in the treatment of congestive heart failure.

Extended outpatient rehabilitation improves independence after hip fracture. Hip fractures are common in the elderly and can have a devastating impact on the ability of older patients to remain independent. Despite standard rehabilitation, up to three-fourths of patients with hip fractures fail to regain their walking ability or functional status within six to twelve months of surgery. To determine whether additional rehabilitation would improve function following hip fracture in frail elders, researchers conducted a randomized controlled trial comparing extended outpatient rehabilitation that included resistance training, to the usual program of low intensity home exercise following surgery to repair a hip fracture. Men and women 65 years or older with a recent hip fracture (within 16 weeks of repair) were randomly assigned to either supervised physical therapy with whole-body progressive resistance exercise training or to a control group doing home exercise focusing primarily on flexibility. The outcome measures included physical performance tests, measures of functional status, and activities of daily living (ADL) over six months. Changes in physical performance and functional status over time were significantly better for the intervention group compared to the control group: patients in the intervention group showed greater improvements in muscle strength, walking speed, and balance than patients in the control group. These results indicate that extended outpatient rehabilitation with progressive resistance training improves physical function and mobility among frail elderly hip fracture patients. Compared to usual care for this patient population, this program promotes better return to pre-fracture function, reduces disability, and improves quality of life.

Early-Life Determinants of Late-Life Health

A number of studies have investigated early-life determinants of later life health. For example, researchers have investigated the association of high blood pressure (BP) and hippocampal atrophy (HA) among Japanese-American men participating in the longitudinal community-based Honolulu Asia Aging Study (HAAS). The hippocampus is an area of the brain that is critical to learning and memory, and is vulnerable to vascular damage. The investigators found that men who had had high midlife BP, but had never been treated, had an increased risk for later HA compared with never-treated men with normal

[11] Data are from the National Center for Health Statistics. See *Morbidity & Mortality: 2004 Chart Book on Cardiovascular, Lung, and Blood Diseases.* National Heart, Lung, and Blood Institute, 2004.

midlife BP. In another study, researchers studying a cohort of young and middle-aged adults from a semi-rural black and white community in Bogalusa, Louisiana, examined the association between carotid wall thickness and traditional cardiovascular risk factors measured since childhood. Increased arterial stiffness is a known predictor of cardiovascular-related diseases and death at middle and older ages, and carotid artery wall thickness is associated with cardiovascular risk factors and predicts atherosclerosis in middle- and older-aged adults. They found that measures of LDL ("bad") cholesterol and relative weight in childhood predicted carotid wall thickness in the adults, and that childhood blood pressure was a consistent predictor of arterial stiffness in adulthood. Recent research has pointed to a number of early life conditions that have far-reaching associations with a range of chronic conditions, including exposure to adverse conditions in utero, infectious diseases and environmental toxins, nutritional deficits, childhood poverty and stressful family conditions. Earlier identification of risk factors that are associated with diseases that manifest later in life could lead to the development of earlier and better preventive strategies.

Elevated levels of homocysteine may be an important but modifiable risk factor for osteoporosis. To test the hypothesis that increased blood homocysteine levels may be a risk factor for osteoporosis, the relationship between circulating homocysteine levels and later hip fractures was evaluated in 825 men and 1174 women, ranging in age from 59 to 91 years, from whom blood samples had been obtained years earlier. After a follow-up of 12.3 years for men and 15.0 years for women, there was a significantly greater risk of hip fracture for both men and women with high homocysteine compared to those with low levels - risk was increased in men and women by a factor of 4 and 1.9 respectively. Because homocysteine levels can be modified by diets or vitamin supplements with sufficient levels of vitamins such as folic acid, B6 and B12, such dietary strategies could reduce the burden of hip fractures in older individuals.

Importance of walking for maintaining mobility. In a recent study of community-dwelling women enrolled in the Women's Health and Aging Study, investigators found that functionally-limited women ages 65 and older, who walked at least eight blocks per week outside their homes, were better able to maintain their functional capacity and walking ability than women who walked less or did not get out the door at all. This effect is independent of initial functional capacity, disease profile, health-related behaviors, and psychological and social-demographic factors. These results provide strong evidence that even a small amount of regular walking can help to maintain mobility.

Appetite and the immune system: A new model. Loss of appetite and decreased food intake are common among the seriously ill. Appetite regulation is complex and involves a number of factors; for example, appetite is suppressed by leptin, a protein found in fat cells, but stimulated by ghrelin, a recently-identified hormone produced by stomach cells. There is also increasing evidence that the immune system is involved, with immune-based proteins known as inflammatory cytokines acting on the nervous system to control appetite. NIH researchers have recently found that, in addition to stomach cells, ghrelin is produced in certain immune cells, along with its receptor protein, GHS-R. When ghrelin binds to GHS-R, the result is inhibition of inflammatory cytokines associated with appetite loss. They further found that leptin increases cytokine activity, while also spurring increased expression of GHS-R by T-lymphocytes, a different type of immune cell. These findings provide a model of how ghrelin and leptin work together to control immune cell activation and inflammation with regard to the appetite, and

also suggest that drugs that stimulate ghrelin/GHS-R may be useful in the management of wasting associated with chronic disease.

BIOLOGY OF AGING

Aging is accompanied by gradual changes in most body systems. Research on the biology of aging focuses on understanding the cellular and molecular processes underlying these changes as well as those accompanying the onset of age-related diseases. As scientists learn more about these processes, experiments can be designed to understand when and how pathological changes begin, providing important clues toward developing interventions to prevent or treat disease. A great deal has been learned about structural and functional changes that occur in different body systems. Research has expanded our knowledge, too, of the biologic factors associated with extended longevity in humans and animal models.

Adult mice continue to produce eggs. One of the basic underpinnings of reproductive biology has been the tenet that the number of oocytes (eggs) in the ovaries of most mammals – including human women – is fixed at birth and declines throughout life, coinciding with a woman's diminishing fertility as she approaches menopause. However, NIH-supported researchers have recently uncovered surprising evidence that egg production in mice may continue on a small scale throughout life. While additional research is needed, the results of this study have called into question decades of scientific thought. The finding that new eggs are produced into adulthood in mice may, if extended to human women, lead to interventions to regulate the rate at which oocytes are formed. This could, in turn, have important implications on the treatment of premature ovarian failure, the extension of fertility, or even the timing of menopause.

Regeneration of skeletal muscle by hematopoietic stem cells. As we age, the ability of our tissues to regenerate in response to injury diminishes, although the mechanisms of this decline are not known. Recently, research results have suggested that therapies that stimulate the body's naturally-occurring stem cells may help in the repair or regeneration of muscle and possibly other tissues. In the first study, researchers found that satellite cells – adult stem cells found in muscle tissue – have an increasingly impaired ability to proliferate with increasing age, and that this is at least partly due to insufficient activation of a protein called Notch. They found that inhibition of Notch impairs muscle regeneration in mice, whereas activation of Notch restores regenerative potential to old muscle, suggesting that Notch is a key factor in muscle regeneration. In the second study, investigators found that a single hematopoietic stem cell is not only able to replenish components of blood, but can also participate in muscle regeneration in mice. Integration of bone marrow-derived cells into myofibers occurs spontaneously at low frequency and increases with muscle damage, suggesting that stem cell therapy might be effective in attenuating age-related muscle dysfunction.

Inherited defects in mitochondrial function contribute to diabetes risk in children of diabetics. Insulin resistance is a metabolic disorder that is thought to precede the development of type 2 diabetes, the most common type of diabetes in adults. The initial manifestations of insulin resistance are abnormally high levels of insulin, as well as levels of glucose in the blood that are higher than normal, but not severe enough to be classified as diabetes. Two important factors noted in the development of insulin resistance are age-related accumulation of fat in skeletal muscle cells and the

dysfunction of mitochondria (cell components responsible for combining oxygen with cellular "fuels" such as fat and sugar to provide usable energy for body functions) in skeletal muscle. Insulin resistance also appears to be involved in the development of diabetes in the offspring of type 2 diabetics.

In a recent study, researchers found that insulin resistance in the young (primarily in their 20s and 30s), lean, offspring of type 2 diabetics was related to increased fat content of muscle and inherited defects in mitochondrial function, suggesting that these alterations may represent the earliest antecedent conditions in the development of type 2 diabetes. Additional studies of early metabolic changes contributing to insulin resistance and diabetes across various ages and within families, especially through the use of non-invasive methods, will be valuable in identifying metabolic problems at the earliest stages and to the development of effective primary prevention strategies for type 2 diabetes.

Extending the Lifespan

Identification of the factors that affect the overall lifespan of an organism will help us better understand the aging process, and will also help us develop interventions to keep older people healthy and free of disease and disability as long as possible. Over the last ten years, the NIA Longevity Assurance Gene (LAG) Initiative has been pivotal in the identification of multiple genes, pathways, and biological processes involved in the regulation of longevity and aging in multiple organisms (yeast, nematode, fruit fly, mouse, and human). Through the use of both invertebrate and mammalian models, the LAG Initiative has identified common factors and mechanisms that mediate longevity and extend health span.

Gene that regulates cholesterol is related to exceptional longevity. Exceptional human longevity tends to run in families. Both environmental and genetic factors may account for this. Previous genetic studies had indicated that variants of two genes that regulate blood cholesterol are found especially frequently in centenarians, suggesting that they contributed in some way to exceptionally long life. Researchers studying Ashkenazi Jewish centenarians and their children (whose average age was 68) found that a variant of a third gene that regulates cholesterol is found much more commonly in the centenarians and their children than in the general population. The variant causes the size of lipoproteins, the particles that carry cholesterol in the blood, to be larger than average (larger lipoproteins are less likely to cause the buildup of plaque along arterial walls), and is associated with high levels of high-density lipoprotein (HDL or "good" cholesterol), which tends to protect against cardiovascular disease. These results reinforce evidence that genetic regulation of cholesterol has important effects on longevity and that certain genetic variants predispose to exceptional longevity. In addition, this study, more than previous ones, provides a link between a particular gene and the mechanism by which it exerts its effects (regulation of HDL cholesterol by control of lipoprotein particle size).

Improved screening for interventions that regulate longevity. The discovery of genes and drugs that affect life span has been delayed by the fact that measuring an organism's life-span is inherently time-consuming and requires a large number of animals. However, researchers have recently developed a much faster assay for interventions that slow down aging in the fruit fly. Using this new screen, life-extending mutations can be identified in only a few weeks. This assay can be used not only to facilitate identification of long-lived mutants, but also to identify pharmacological

interventions that increase longevity; for example, using this assay, investigators found that the anti-oxidant lipoic acid, but not vitamin E, extends fruit fly life span.

Story of Discovery: Eat, Drink, and Live Longer? Caloric Restriction, Sirtuins, and Longevity

In 1513, the Spanish explorer Juan Ponce de León began his search for the fabled "fountain of youth," a spring whose waters were said to confer eternal life and boundless good health upon anyone who drank from it. Although Ponce de León's quest was not a complete failure – he did discover the Florida peninsula – he did not, ultimately, find what he was looking for. The idea of a fountain of youth eventually receded into myth.

However, the idea of an intervention that may extend both life and health (for a while, if not indefinitely) has gained legitimacy over the past century. With extensive NIH support, researchers have been investigating both genetic and environmental influences on healthy aging and longevity, as well as the interplay between them. Recently, NIH-supported researchers have discovered a family of cellular enzymes that will, under certain conditions, retard cellular aging and delay cellular death. They have also identified at least one compound that activates these enzymes and that significantly extends the lifespan of several experimental models as a result – and they have demonstrated that this compound exists in a number of common foods. Although additional research is needed, scientists are optimistic that the ability to simultaneously extend the lifespan and safeguard health may not be a myth after all.

Ironically, the discoveries of this family of life-extending enzymes, called *sirtuins*, and the food-derived compound that stimulates them are rooted in studies of food deprivation. In 1914, eventual Nobel laureate Francis Peyton Rous published a paper showing that reduction of food intake retards carcinogenesis in rats. Although Rous's work did not directly address the question of longevity, he was the first of many researchers to demonstrate a clear health benefit from caloric restriction (CR), or reducing an organism's caloric intake while ensuring adequate intake of essential nutrients. In fact, later research would show that CR also slows progression of kidney disease and protects against autoimmune disease in rodent models. In 1935, the pioneering work of McCay et al. showed that CR rats lived much longer than others, and research in the 1940s and 1950s extended these findings to other species, including invertebrates such as yeast and worms, which are today a major source of important data on aging.

Research in this area continued over the next several decades, with a number of theories proposed as to how and why CR extends the lifespan. Investigators discovered that CR animals have low levels of circulating insulin and an increased daily peak in certain stress hormones, a finding that led them to propose a theory for how CR extends life: as a mild form of chronic stress, it may prepare organisms to cope more effectively at the physiologic level with more intense stresses, including age-related oxidative damage.

Meanwhile, a separate group, this one working with yeast, was beginning to uncover the biological mechanisms through which CR may function. In 1997, this NIH-supported team discovered that a gene called sir2, for silent information regulator, recognizes food deprivation within the cells – in yeast, at least – and sets into motion the changes that increase the organism's lifespan. When faced with a stressor (such as food deprivation) sir2 activates sirtuins, which prevent cell death by enhancing DNA repair processes and production of protective antioxidants. Research findings from last year suggest that similar mechanisms work in rodent and human cells, in which CR activates SIRT-1, the mammalian form of sir2. The case for sirtuins as key to CR's ability to extend life was also strengthened by the finding that CR does not extend life in animals that have been genetically altered to lack sirtuins.

Because an intensive regimen of restricted food intake may prove too difficult for most people to follow over the long term, investigators are now searching for compounds that mimic CR. Last year, NIH-supported researchers identified several compounds that increase both sir2 activity and longevity in yeast. The most potent activator of sir2 identified so far is resveratrol, a compound found in many foods – notably red wine, but also in grapes, mulberries, and peanuts. Resveratrol also appears to increase longevity in nematodes and fruit flies. The researchers theorize that sir2 expression and activity, as stimulated by resveratrol, mimic the mild stress induced in yeast by caloric restriction, essentially sending out a "false alarm" that tricks the cell into thinking it is starving and setting into motion the cell-protective events described above.

Whether such an intervention would work in mammals has not yet been tested, but diet supplementation with these compounds may be effective against a number of potentially debilitating conditions in humans. For example researchers have

uncovered intriguing hints that sirtuins may affect the cells' capacity for fat storage, perhaps working through the insulin/IGF signaling pathway, which is known to influence lifespan in a number of lower organisms, including rodents. This would suggest that compounds that activate sirtuins and SIRT-1 may be useful in treating obesity and the problems associated with type 2 diabetes.

Ponce de León traveled all the way to Florida to seek the fountain of youth. Will tomorrow's intrepid explorer need venture only as far as his or her medicine cabinet – or kitchen? It's far too early to make such a prediction. For one thing, there have been no clinical studies of resveratrol or related compounds in humans; interventions that are effective in yeast and rats may be less effective, or have unexpected side effects, in higher organisms. Even if such compounds do work, it's hard to know exactly how many years they will add to the average human lifespan, although interventions that increase longevity in rodents typically do so by about 30 percent. Even CR itself remains to be scientifically validated as a useful intervention for healthy aging and longevity in humans, although research results to date have been somewhat promising. Compounds that stimulate sirtuin activity, whether ingested through a pill or through a nightly glass of cabernet, may one day be widely recommended as a way to increase the odds of enjoying a longer life accompanied by a longer period of good health.

Initiatives: Biology of Aging

The identification of "longevity genes" is complex and necessarily interdisciplinary, involving ongoing interactions between basic and epidemiologic researchers to accelerate discovery of, and confirm, translational findings. To facilitate identification and understanding of longevity genes, the NIA has formed the Longevity Consortium - a system for rapid generation, review, and funding of new projects. Components of the Consortium include multiple basic laboratories addressing relevant disciplines including cell and molecular biology, physiology, and biochemistry; diverse populations and large sample sizes to allow analyses of subgroups and covariates; registry and/or database capacity to allow rapid identification of possible cases and controls, and genotype and phenotype information; and genotyping, genomics, computational, and cell line repository facilities to allow standardization and economies of scale. The Consortium provides a system for rapid information exchange among basic and epidemiologic researchers to convey new findings and conduct follow-up studies, as well as for rapid review and funding to allow faster start-up of basic or epidemiologic studies on new alleles of interest.

Members of the Consortium include epidemiologists, geneticists, population biologists, statisticians, and others with an interest in the genetic and molecular basis for longevity, and draws on the study populations of 15 of the largest human aging studies, including the Cardiovascular Health Study, the Women's Health Initiative, Health ABC, the Study of Osteoporotic Fractures, the Rotterdam Study, the Honolulu Heart Study, and the New England Centenarian Study. Altogether, Consortium researchers will have access to data on some 200,000 study subjects. Through this Consortium, it is expected that basic science discoveries will lead to tests of hypotheses in human populations, and observations in populations will, in turn, suggest tests of biologic mechanisms.

BEHAVIORAL AND SOCIAL RESEARCH

Behavioral and lifestyle factors have a profound impact on health throughout the life span. For example, older adults can help to prevent disease and disability and improve their quality of life through healthy behaviors such as proper nutrition and exercise, use of preventive health care, and avoiding smoking and alcohol abuse. NIA research on behavioral and social factors in aging encompasses a number of areas, including economic implications of aging at both the personal and societal levels, the effects of behavior and attitude on health, and the demographics of aging.

The role of public "report cards" in medical markets. In recent years, public "report card" programs have been started by both private and public organizations to supply information regarding the quality of medical care provided by hospitals and physicians. By supplying patients and referring physicians with more information when making decisions about where to receive care, report cards can be advantageous. They can also provide hospitals with information that could be used as a guideline to improving care. However, report cards could also create problems. If the performance measures fail to account for the underlying health of the patients being treated, then the measure of performance might reflect more the existing health problems of patients served by a particular hospital than the actual quality of care being rendered. This could lead to flawed decision-making by patients and referring physicians based on poor data, as well as causing hospitals to become less willing to serve particularly high-risk patients in order to avoid having their reputations penalized. Recently, researchers used Cardiac Surgery Reporting System (CSRS) data from New York State to evaluate the impact of report cards on the distribution of where patients go for bypass surgery, and whether good or bad reports lead to improvements in the quality of care, measured by mortality. In their study, being reported as a poor performer ("high mortality") was associated with a 10 percent reduction in bypass-surgery patients per month in the 12 months following the report. The shift appeared to be primarily due to patients and referring doctors choosing to have procedures performed at low-mortality hospitals. However, the researchers found that hospitals flagged as poor performers improve patient mortality by 1.2 percentage points within the 12 month period following the report. Since this study took into account the severity of patient condition, the latter change does not appear to be simply due to sicker patients moving to low mortality hospitals. Indeed, the findings show that low-performing hospitals lose relatively healthy patients to competing facilities. While additional research is needed to identify exactly what mechanisms underlie the reported changes, the findings do provide evidence that report cards could have a beneficial impact on the quality of healthcare.

Separate neural systems value immediate and delayed monetary rewards. When given a choice in the "here-and-now," people frequently choose courses of action that lead to immediate rewards, while making very different choices when considering future actions. For example, it is well-established that people often express great eagerness to quit smoking, initiate an exercise program, or begin to contribute to a retirement savings plan...tomorrow. In a recent study, investigators used functional magnetic resonance imaging (fMRI) to measure the brain activity of participants as they chose between an *immediate* monetary reward and a *later* monetary reward. They found that when the participant considered the immediate reward, the brain's limbic system, which is implicated in "emotional" brain processes, was activated, while the more cognitively-oriented lateral prefrontal cortex was activated when the participants considered the longer-term reward. These results converge with those of a series of recent imaging studies that have examined interactions between prefrontal cortex and limbic mechanisms in a variety of behavioral contexts, ranging from economic and moral decision making to more visceral responses such as pain. Collectively, these studies suggest that human behavior is often governed by a competition between lower level, automatic processes, which may reflect evolutionary adaptations to particular environments, and the more recently evolved, uniquely human capacity for abstract general reasoning and future planning.

HEALTH DISPARITIES RESEARCH

The health status of racial and ethnic minority groups in the U.S. has improved steadily over the last century. Despite such progress, disturbing disparities in health persist between majority and minority populations. Demographic projections predict a substantial change in the racial and ethnic makeup of the older population, heightening the need to examine and reduce differences in health and life expectancy.

Assessing cognitive differences. Census data indicate that in the United States, Latinos have become the largest ethnic minority group, and it is important to understand their health needs. However, it may be difficult to assess the incidence of age-related conditions, particularly cognitive impairment, in this population, as many relevant neuropsychological instruments are inappropriate for studies of older Latinos. Last year investigators found that one test, the Spanish English Verbal Learning Test, is a valid and sensitive measure of cognitive functioning. More recently, the researchers determined that there may be a similar pattern of cognitive declines for verbal memory and expressive language and findings on brain imaging that predict declines in everyday functioning in both Hispanic and Caucasian older adults.

Racial differences in family caregiving. Resources for Enhancing Alzheimer's Caregiver Health (REACH) is a unique, two phase, multisite research program sponsored by the NIA and the National Institute on Nursing Research to carry out social and behavioral research on interventions designed to enhance family caregiving for AD and related disorders. Recently, REACH investigators published two companion papers addressing the issue of racial differences in family caregiving. In one analysis, African-American caregivers reported lower anxiety, better well-being, less use of psychotropic medications, more benign appraisals of stress and perceived benefits of caregiving, and greater religious coping and participation than white caregivers. In the other study, Latina caregivers reported lower appraisals of stress, greater perceived benefits of caregiving, and greater use of religious coping than white caregivers. In addition, several differences emerged between less and more acculturated Latinas, emphasizing the need to examine heterogeneity among Latino caregivers.

The NIA is initiating a new project, "Promoting Research Participation Among Black and Hispanic Seniors." Through data analyses, interviews of informed community members, and focus group discussions, this year-long project at the Yale-Older Americans Independence Center will identify characteristics of Black and Hispanic study participants and non-participants and develop recommended practices to improve and promote the recruitment and retention of Black and Hispanic older adults in aging-related research and studies of geriatric health conditions.

INNOVATIONS IN COMMUNICATIONS

NIHSeniorHealth.gov. Last year, the NIH launched NIHSeniorHealth.gov, a unique web site geared toward the health needs of older adults. Developed by the NIA and the National Library of Medicine, the content of this web site is easy for older persons to read, understand, remember, and navigate, using large print and short, easy-to-read segments of information repeated in a variety of formats -- such as open-captioned videos and short quizzes -- to increase the likelihood that it will be remembered. The site also has a "talking" function, allowing users the option of having the text read to them. The content

focuses on health topics of particular interest to older people - AD and AD caregiving, arthritis, hearing loss, and several common types of cancer - and will be regularly expanded and updated.

In its first year, NIHSeniorHealth.gov was extremely successful, attracting some 380,000 unique visitors and garnering over three million page views. It was also one of six programs, and the only web site, to receive an "Industry Innovators Award" from the International Council on Active Aging. Recent innovations include a "printer-friendly" version of the on-line text, as well as more text sizing options. A "Share a Senior Exercise Story" feature, in which older adults will be invited to send in their stories and photos to serve as an inspiration to others, is planned, and a Spanish-language version of the site is also under development.

Meals on Wheels Initiative. During a 2002 Congressional hearing, it was recommended that NIA and the Administration on Aging (AoA) work together to disseminate research-based consumer education materials to the thousands of seniors who participate in the Meals-on-Wheels (MOW) program across the Nation. In participation with AoA, NIA conducted focus groups with the MOW Association of America to identify the types of information of greatest interest to MOW's clients and the best ways to deliver such information. Now, a new booklet entitled "*Take Your Medicines the Right Way – Everyday!*", as well as a plastic cup with the same message, are being made available to MOW providers for their clients free of charge. The booklet is in easy-to-read language and covers important steps to help ensure safe and effective medication use.

CONCLUSION: Meeting New Challenges through Aging Research

As our population rapidly grows older, it is ever more urgent that we find effective ways to address the often devastating diseases and conditions associated with advanced age. Since the NIA's founding in 1974, groundwork has been laid for today's important advances in understanding basic aging, preventing disease and disability, including AD, and defining special social and behavioral issues for older individuals, their families and caregivers, and clinicians. The latest studies provide additional basic understandings as well as improved interventions to treat, and even prevent, some of the more devastating and disabling aspects of aging. With such research continued and intensified, we can move forward in meeting the promise of a healthy old age by improving the health and well being of older people in America.

The NIH Neuroscience Blueprint

Overview -- The Blueprint is a framework to enhance cooperation among fourteen NIH Institutes and Centers that support research on the nervous system. Over the past decade, driven by the science, the NIH neuroscience Institutes and Centers have increasingly joined forces through initiatives and working groups focused on specific disorders. The Blueprint builds on this foundation, making collaboration a day-to-day part of how the NIH does business in neuroscience. By pooling resources and expertise, the Blueprint can take advantage of economies of scale, confront challenges too large for any single Institute, and develop research tools and infrastructure that will serve the entire neuroscience community.

FY2005 -- For fiscal year 2005, the Blueprint participants are developing an initial set of initiatives focused on tools, resources, and training that can have a quick and substantial impact because each

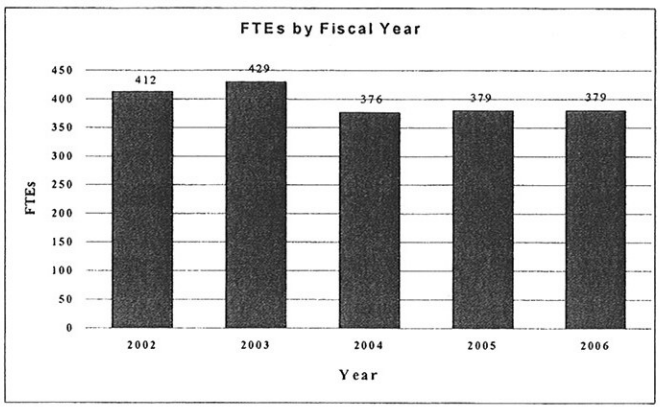
builds on existing programs. These initiatives, with the participation of all Blueprint Institutes, include an inventory of neuroscience tools funded by the NIH and other government agencies, enhancement of training in the neurobiology of disease for basic neuroscientists, and expansion of ongoing gene expression database efforts. The NIA has been an active member in this initiative, and participates in the expansion of the ongoing Gene Expression Nervous System Atlas (GENSAT) and microarray consortium projects, as well as in the development of supplements to training grants to include course work on specific diseases of the brain. In addition, the NIA has a special emphasis upon the neurodegenerative diseases, such as Alzheimer's disease, which occur predominantly later in life. Current NIA initiatives, such as the Alzheimer 's Disease Neuroimaging Initiative, a multi-site, longitudinal, prospective, naturalistic study of normal cognitive aging, mild cognitive impairment, and early Alzheimer's disease, can provide bases upon which Blueprint initiatives can develop.

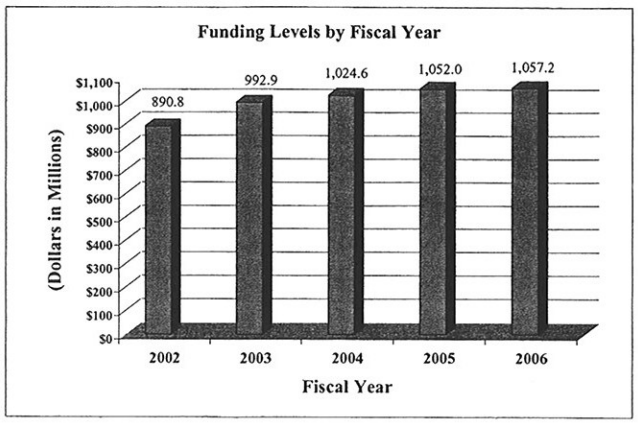
FY2006 -- Advances in the neurosciences and the emergence of powerful new technologies offer many opportunities for Blueprint activities that will enhance the effectiveness and efficiency of neuroscience research. Blueprint initiatives for fiscal year 2006 will include systematic development of genetically engineered mouse strains of critical importance to research on nervous system and its diseases and training in critical cross cutting areas such as neuroimaging and computational biology. The NIA will work with the other Blueprint Institutes on new initiatives such as the Neuromouse Project, which will investigate the function of each gene in the mouse brain, the training of physicians and scientists in translational opportunities in the neurobiology of disease, and the development of neuroscience resource cores to provide regional centers for access to specialized technologies for research on the brain. The NIA will also continue to work with NINDS and NIMH on the Cognitive and Emotional Health Project part of the Neuroepidemiology Initiative.

Budget Policy

The Fiscal Year 2006 budget request for the NIA is $1,057,203,000, an increase of $5,213,000 and 0.5% over the FY 2005 Appropriation. Also included in the FY 2006 request, is NIA's support for the trans-NIH Roadmap initiatives, estimated at 0.89% of the FY 2006 budget request. This Roadmap funding is distributed through the mechanisms of support, consistent with the anticipated funding for the Roadmap initiatives. A full description of this trans-NIH program may be found in the NIH Overview. NIA is participating in the NIH Neuroscience Blueprint. The Fiscal Year 2006 request includes $1,400,000 for a variety of Neuroscience Blueprint initiatives, including neuroscience cores, training initiative, and the Neuromouse project.

A five year history of FTEs and Funding Levels for NIA are shown in the graphs below.



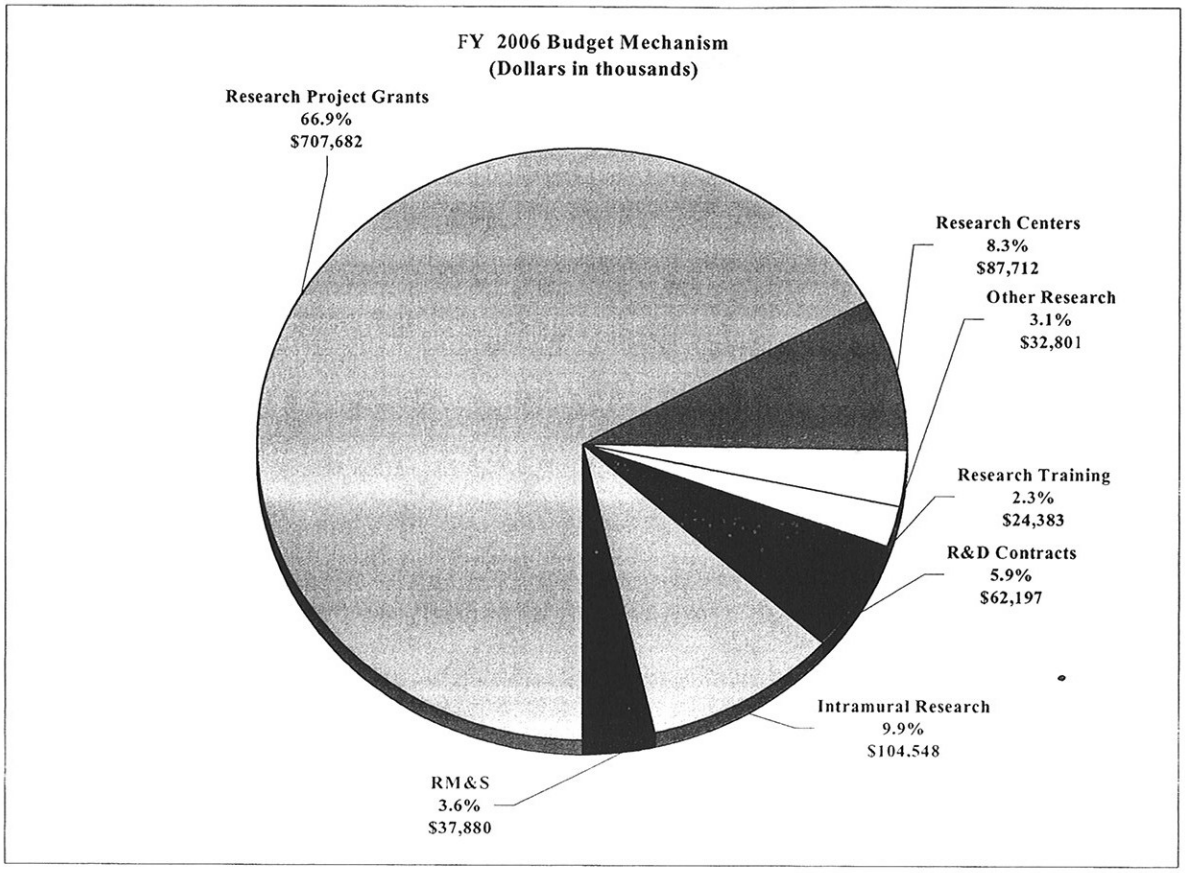


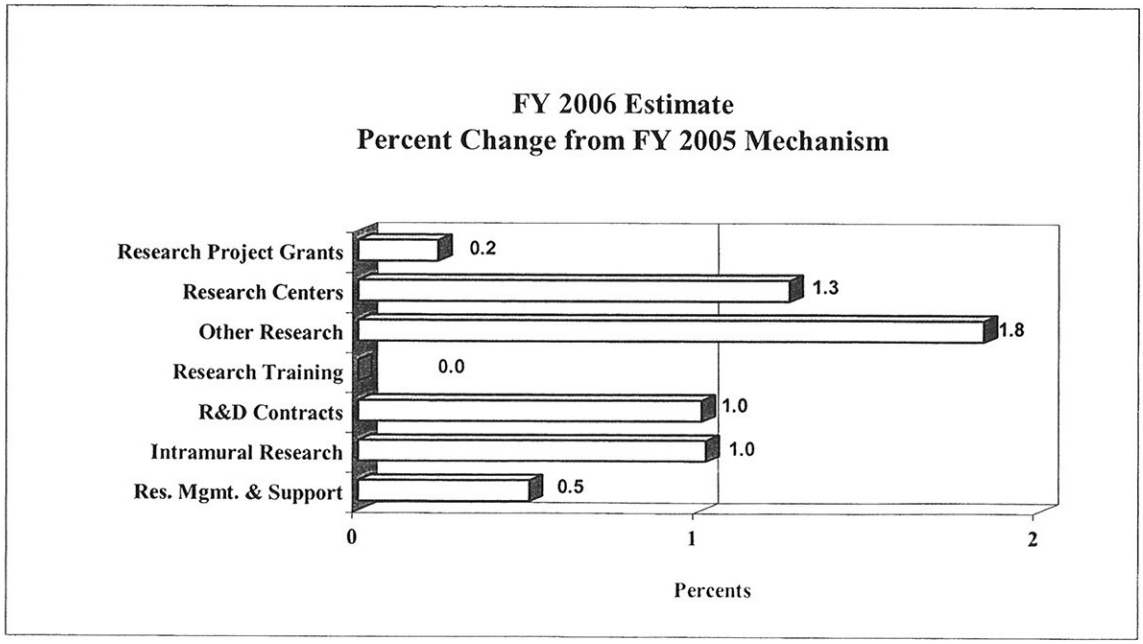
NIH's highest priority is the funding of medical research through research project grants (RPGs). Support for RPGs allows NIH to sustain the scientific momentum of investigator-initiated research while pursuing new research opportunities. The average cost of competing RPGs will be held at the FY 2005 level. There will be no inflationary increases for direct, recurring costs in Noncompeting continuation RPGs.

Advancement in medical research is dependent on attracting the best and the brightest to pursue careers in biomedical research. In the Fiscal Year 2006 request, stipend levels for post-doctoral recipients supported through the Ruth L. Kirschstein National Research Service Awards will increase by 4.0% for those with 1-2 years of experience, with all other stipends remaining at the FY 2005 levels. NIH will also provide an increase of $500 per post-doctoral fellow, for increased health insurance costs. This increase in stipends and health benefits is financed within the FY 2006 request by reducing the number of Full-Time Training Positions by 2. NIA will support 541 pre- and postdoctoral trainees in full-time training positions.

The Fiscal Year 2006 request includes funding for 76 research centers, 236 other research grants, including 206 clinical career awards, and 133 R&D contracts. Intramural Research will receive a 1% increase and Research Management and Support will receive an increase of 0.5 percent, the same as the NIH total increase.

The mechanism distribution by dollars and percent change are displayed below:





NATIONAL INSTITUTES OF HEALTH
National Institute on Aging

Budget Mechanism - Total

MECHANISM	FY 2004 Actual		FY 2005 Appropriation		FY 2006 Estimate	
Research Grants:	No.	Amount	No.	Amount	No.	Amount
Research Projects:						
Noncompeting	973	$493,907,000	1,090	$534,499,000	1,032	$519,544,000
Administrative supplements	(103)	7,084,000	(103)	7,079,000	(103)	7,079,000
Competing:						
Renewal	77	58,106,000	69	48,369,000	78	54,678,000
New	336	106,979,000	280	91,151,000	312	101,454,000
Supplements	6	1,109,000	0	0	0	0
Subtotal, competing	419	166,194,000	349	139,520,000	390	156,132,000
Subtotal, RPGs	1,392	667,185,000	1,439	681,098,000	1,422	682,755,000
SBIR/STTR	87	24,535,000	87	24,927,000	87	24,927,000
Subtotal, RPGs	1,479	691,720,000	1,526	706,025,000	1,509	707,682,000
Research Centers:						
Specialized/comprehensive	76	83,330,000	76	86,615,000	76	86,784,000
Clinical research	0	0	0	0	0	0
Biotechnology	1	428,000	0	0	1	928,000
Comparative medicine	0	0	0	0	0	0
Research Centers in Minority Institutions	0	0	0	0	0	0
Subtotal, Centers	77	83,758,000	76	86,615,000	77	87,712,000
Other Research:						
Research careers	194	25,213,000	204	25,601,000	206	26,017,000
Cancer education	0	0	0	0	0	0
Cooperative clinical research	3	1,728,000	2	993,000	2	993,000
Biomedical research support	0	19,000	0	25,000	0	28,000
Minority biomedical research support	0	1,338,000	0	1,365,000	0	1,365,000
Other	29	3,908,000	28	4,225,000	28	4,398,000
Subtotal, Other Research	226	32,206,000	234	32,209,000	236	32,801,000
Total Research Grants	1,782	807,684,000	1,836	824,849,000	1,822	828,195,000
Research Training:	FTTPs		FTTPs		FTTPs	
Individual awards	62	2,610,000	62	2,717,000	61	2,717,000
Institutional awards	488	21,132,000	481	21,666,000	480	21,666,000
Total, Training	550	23,742,000	543	24,383,000	541	24,383,000
Research & development contracts	132	56,797,000	132	61,576,000	133	62,197,000
(SBIR/STTR)	(0)	(49,000)	(0)	(52,000)	(0)	(0)
	FTEs		FTEs		FTEs	
Intramural research	261	99,962,000	261	103,491,000	261	104,548,000
Research management and support	115	36,413,000	118	37,691,000	118	37,880,000
Cancer prevention & control	0	0	0	0	0	0
Construction		0		0		0
Buildings and Facilities		0		0		0
Total, NIA	376	1,024,598,000	379	1,051,990,000	379	1,057,203,000
(RoadMap Support)		(3,519,000)		(6,651,000)		(9,454,000)
(Clinical Trials)		(76,085,000)		(78,139,000)		(78,530,000)

NATIONAL INSTITUTES OF HEALTH
National Institute on Aging

Budget Authority by Activity
(dollars in thousands)

ACTIVITY	FY 2004 Actual		FY 2005 Appropriation		FY 2006 Estimate		Change	
	FTEs	Amount	FTEs	Amount	FTEs	Amount	FTEs	Amount
Extramural Research:								
Aging		$888,223		$910,808		$914,775		$3,967
Subtotal, Extramural research		888,223		910,808		914,775		3,967
Intramural research	261	99,962	261	103,491	261	104,548	0	1,057
Res. management & support	115	36,413	118	37,691	118	37,880	0	189
Total	376	1,024,598	379	1,051,990	379	1,057,203	0	5,213

NATIONAL INSTITUTES OF HEALTH
National Institute on Aging

Summary of Changes

FY 2005 Estimate				$1,051,990,000
FY 2006 Estimated Budget Authority				1,057,203,000
Net change				5,213,000
	FY 2005 Appropriaton		Change from Base	
CHANGES	FTEs	Budget Authority	FTEs	Budget Authority
A. Built-in:				
1. Intramural research:				
a. Within grade increase		$35,490,000		$468,000
b. Annualization of January 2005 pay increase		35,490,000		327,000
c. January 2006 pay increase		35,490,000		623,000
d. One less day of pay		35,490,000		(136,000)
e. Payment for centrally furnished services		11,506,000		54,000
f. Increased cost of laboratory supplies, materials, and other expenses		56,495,000		1,034,000
Subtotal				2,370,000
2. Research Management and Support:				
a. Within grade increase		15,000,000		257,000
b. Annualization of January 2005 pay increase		15,000,000		138,000
c. January 2006 pay increase		15,000,000		265,000
d. One less day of pay		15,000,000		(57,000)
e. Payment for centrally furnished services		5,004,000		26,000
f. Increased cost of laboratory supplies, materials, and other expenses		17,687,000		326,000
Subtotal				955,000
Subtotal, Built-in				3,325,000

NATIONAL INSTITUTES OF HEALTH
National Institute on Aging

Summary of Changes--continued

CHANGES	2005 Current Estimate Base		Change from Base	
	No.	Amount	No.	Amount
B. Program:				
1. Research project grants:				
a. Noncompeting	1,090	$541,578,000	(58)	($14,955,000)
b. Competing	349	139,520,000	41	16,612,000
c. SBIR/STTR	87	24,927,000	0	0
Total	1,526	706,025,000	(17)	1,657,000
2. Research centers	76	86,615,000	1	1,097,000
3. Other research	234	32,209,000	2	592,000
4. Research training	543	24,383,000	(2)	0
5. Research and development contracts	132	61,576,000	1	621,000
Subtotal, extramural				3,967,000
	FTEs		FTEs	
6. Intramural research	261	103,491,000	0	(1,313,000)
7. Research management and support	118	37,691,000	0	(766,000)
Subtotal, program		1,051,990,000		1,888,000
Total changes	379		0	5,213,000

NATIONAL INSTITUTES OF HEALTH
National Institute on Aging

Budget Authority by Object

	FY 2005 Appropriation	FY 2006 Estimate	Increase or Decrease
Total compensable workyears:			
Full-time employment	379	379	0
Full-time equivalent of overtime & holiday hours	1	1	0
Average ES salary	$149,608	$153,049	$3,441
Average GM/GS grade	10.9	10.9	0.0
Average GM/GS salary	$73,502	$75,192	$1,690
Average salary, grade established by act of July 1, 1944 (42 U.S.C. 207)	$91,084	$93,179	$2,095
Average salary of ungraded positions	111,517	114,082	2,565

OBJECT CLASSES	FY 2005 Appropriation	FY 2006 Estimate	Increase or Decrease
Personnel Compensation:			
11.1 Full-Time Permanent	$21,159,000	$21,949,000	$790,000
11.3 Other than Full-Time Permanent	10,530,000	10,923,000	393,000
11.5 Other Personnel Compensation	1,093,000	1,134,000	41,000
11.7 Military Personnel	544,000	565,000	21,000
11.8 Special Personnel Services Payments	8,033,000	8,333,000	300,000
Total, Personnel Compensation	41,359,000	42,904,000	1,545,000
12.0 Personnel Benefits	8,744,000	9,070,000	326,000
12.1 Military Personnel Benefits	387,000	401,000	14,000
13.0 Benefits for Former Personnel	0	0	0
Subtotal, Pay Costs	**50,490,000**	**52,375,000**	**1,885,000**
21.0 Travel & Transportation of Persons	1,509,000	1,500,000	(9,000)
22.0 Transportation of Things	209,000	200,000	(9,000)
23.1 Rental Payments to GSA	1,000	1,000	0
23.2 Rental Payments to Others	2,866,000	2,949,000	83,000
23.3 Communications, Utilities & Miscellaneous Charges	1,154,000	1,187,000	33,000
24.0 Printing & Reproduction	620,000	638,000	18,000
25.1 Consulting Services	1,441,000	1,483,000	42,000
25.2 Other Services	11,968,000	12,315,000	347,000
25.3 Purchase of Goods & Services from Government Accounts	65,806,000	66,935,000	1,129,000
25.4 Operation & Maintenance of Facilities	6,168,000	6,347,000	179,000
25.5 Research & Development Contracts	34,191,000	35,083,000	892,000
25.6 Medical Care	402,000	413,000	11,000
25.7 Operation & Maintenance of Equipment	2,226,000	2,291,000	65,000
25.8 Subsistence & Support of Persons	0	0	0
25.0 Subtotal, Other Contractual Services	**122,202,000**	**124,867,000**	**2,665,000**
26.0 Supplies & Materials	9,926,000	9,900,000	(26,000)
31.0 Equipment	11,018,000	11,000,000	(18,000)
32.0 Land and Structures	0	0	0
33.0 Investments & Loans	0	0	0
41.0 Grants, Subsidies & Contributions	851,987,000	852,578,000	591,000
42.0 Insurance Claims & Indemnities	0	0	0
43.0 Interest & Dividends	8,000	8,000	0
44.0 Refunds	0	0	0
Subtotal, Non-Pay Costs	**1,001,500,000**	**1,004,828,000**	**3,328,000**
Total Budget Authority by Object	**1,051,990,000**	**1,057,203,000**	**5,213,000**

NATIONAL INSTITUTES OF HEALTH
National Institute on Aging

Salaries and Expenses

OBJECT CLASSES	FY 2005 Appropriation	FY 2006 Estimate	Increase or Decrease
Personnel Compensation:			
Full-Time Permanent (11.1)	$21,159,000	$21,949,000	$790,000
Other Than Full-Time Permanent (11.3)	10,530,000	10,923,000	393,000
Other Personnel Compensation (11.5)	1,093,000	1,134,000	41,000
Military Personnel (11.7)	544,000	565,000	21,000
Special Personnel Services Payments (11.8)	8,033,000	8,333,000	300,000
Total Personnel Compensation (11.9)	**41,359,000**	**42,904,000**	**1,545,000**
Civilian Personnel Benefits (12.1)	8,744,000	9,070,000	326,000
Military Personnel Benefits (12.2)	387,000	401,000	14,000
Benefits to Former Personnel (13.0)	0	0	0
Subtotal, Pay Costs	**50,490,000**	**52,375,000**	**1,885,000**
Travel (21.0)	1,509,000	1,500,000	(9,000)
Transportation of Things (22.0)	209,000	200,000	(9,000)
Rental Payments to Others (23.2)	2,866,000	2,949,000	83,000
Communications, Utilities and Miscellaneous Charges (23.3)	1,154,000	1,187,000	33,000
Printing and Reproduction (24.0)	620,000	638,000	18,000
Other Contractual Services:			
Advisory and Assistance Services (25.1)	1,441,000	1,483,000	42,000
Other Services (25.2)	11,968,000	12,315,000	347,000
Purchases from Govt. Accounts (25.3)	15,607,000	16,628,000	1,021,000
Operation & Maintenance of Facilities (25.4)	6,168,000	6,347,000	179,000
Operation & Maintenance of Equipment (25.7)	2,226,000	2,291,000	65,000
Subsistence & Support of Persons (25.8)	0	0	0
Subtotal Other Contractual Services	**37,410,000**	**39,064,000**	**1,654,000**
Supplies and Materials (26.0)	9,926,000	9,900,000	(26,000)
Subtotal, Non-Pay Costs	53,694,000	55,438,000	1,744,000
Total, Administrative Costs	**104,184,000**	**107,813,000**	**3,629,000**

NATIONAL INSTITUTES OF HEALTH

National Institute on Aging

SIGNIFICANT ITEMS IN HOUSE, SENATE, AND CONFERENCE APPROPRIATIONS COMMITTEE REPORTS

FY 2005 House Appropriations Committee Report Language (H. Rpt. 108-636)

Item

Alzheimer's Disease – The number of Americans with Alzheimer's – 4.5 million today – will increase to between 11.2 million and 16 million by 2050. Within a decade, total annual Medicare costs for people with Alzheimer's will increase by almost 55 percent to nearly $50 billion. The Committee notes that rapid advances in basic science are helping to identify multiple targets for therapies that may help slow or halt the progression of Alzheimer's disease. Before these promising advances can be put to use preventing or treating the disease, they must be tested and validated in controlled clinical trials. The Committee encourages NIA to launch simultaneous clinical trials on therapies it determines to be most promising. The Committee also encourages NIA to work collaboratively with other institutes and the CDC to educate Americans about the ways they can maintain their brain as they age. (p. 90)

Action taken or to be taken

The NIA is taking a multi-pronged approach to developing an intervention to treat Alzheimer's disease (AD) that pursues both behavioral and pharmacological interventions and, in the case of the latter, approaches a variety of suspected disease mechanisms simultaneously. The NIA has more than two dozen clinical trials investigating non-behavioral interventions for AD or related cognitive impairment. Trials currently enrolling patients include studies of: the non-steroidal anti-inflammatory medications naproxen and celecoxib to delay or prevent the onset of AD and age-related cognitive decline; Simvastatin®, a cholesterol lowering drug or statin, to test whether using a cholesterol lowering medication can slow disease progress in people with mild to moderate AD; selenium and/or vitamin E supplements to prevent memory loss and dementia, such as AD (an addition to the NCI prevention trial on prostate cancer); high-dose folate (folic acid), vitamin B6, and vitamin B12 supplementation to determine if reduction of homocysteine levels will slow the rate of cognitive decline in AD; valproate (an anticonvulsant) to delay the emergence of agitation and/or psychosis in persons with probable AD; vitamin E to slow the rate of cognitive/functional decline or development of AD in older persons with Down syndrome; huperzine A, a natural cholinesterase inhibitor with antioxidant and neuroprotective properties derived from the Chinese herb Huperzia serrata, to improve cognitive function in individuals with AD; and nicotine, using patches, to improve or delay the progression of symptoms in mild cognitive impairment.

The NIA continues to work collaboratively with other institutes, federal agencies, and private and professional organizations to support research and disseminate information on ways to maintain a healthy brain as one ages. The Cognitive and Emotional Health Project (CEHP) is a joint venture of three Institutes - NIA, NIMH, and NINDS; the overarching goal is to determine how cognitive and

emotional health can be maintained and enhanced as people age, by assessing the state of the science on various determinants of adult cognitive and emotional health, and by promoting research to accelerate the pace of scientific advances. In 2004, the Alzheimer's Association launched a national campaign about AD, which includes a program urging people to "Maintain Your Brain." This program is based on the best available science about brain health, which continues to emerge from studies supported by the NIA and other NIH institutes. The healthy lifestyles and nutrition emphasized in the "Maintain your Brain" program are also part of the health promotion program of the CDC on aging and elderly health, which includes the *National Blueprint: Increasing Physical Activity Among Adults Aged 50 and Older.* The NIA participated in the National Blueprint Steering Committee, and will continue to pursue opportunities for CDC collaboration on educational activities about ways to maintain a healthy brain.

Item

Down syndrome – Research has shown that many people with Down syndrome develop the neuropathological findings of Alzheimer's disease, and that many go on in later life to show cognitive decline. The Committee encourages NIA to study the connection between Alzheimer's disease and Down syndrome and to work closely with NINDS, NICHD, NIMH and NHGRI to establish an initiative to support Down syndrome research on improving cognition and preventing early dementia through biomedical treatments. (p. 90)

Action taken or to be taken

Down Syndrome is due to trisomy (three copies) of chromosome 21 and involves misexpression of hundreds of genes. Recent work in Down syndrome mouse models suggests that certain individual genes on chromosome 21 are particularly critical to producing the overall phenotype. One of these genes involves amyloid precursor protein (APP), which is of particular interest to NIA, since amyloid plaques (one of the pathological hallmarks of Alzheimer's disease) are formed through the accumulation and aggregation of beta-amyloid peptides derived from APP.

The NIA is currently supporting two clinical trials addressing Down syndrome. One is a multi-national trial of vitamin E in older Down syndrome individuals to evaluate cognitive and functional changes. The second is a pilot trial of the combination of vitamin E/vitamin C/alpha-lipoic acid in older Down syndrome individuals to determine whether certain cognitive measure are improved with the intervention.

The NIA is also coordinating with NINDS, which is planning a workshop to discuss recent findings and explore the basic biology of Down syndrome and begin to identify some potential therapeutic targets. The workshop is aimed at identifying such targets or at establishing what knowledge or technical barriers need to be overcome in order to advance toward this goal. Quite a few specific synaptic defects have now been identified in Down syndrome patients and model mice, including APP toxicity. In addition, it is hoped that the workshop will help attract new researchers with basic neuroscience background into the study of Down syndrome. The NIA will work closely with other institutes, including NICHD, NIMH, and NHGRI, when new initiatives are developed.

Item

End-of-life/palliative care – The Committee encourages NIA to expand research, implementation of insights in practice, and training programs, aiming to understand the mechanisms of disability and suffering in fatal chronic illness and to prevent and relieve that disability and suffering, particularly with respect to pain management. (p. 90)

Action taken or to be taken

Understanding the mechanisms of disability and suffering in both fatal and non-fatal chronic illnesses is a major area of research emphasis for the NIA, which supports a wide range of research and training to understand these mechanisms and to prevent and relieve related disability and suffering, particularly with respect to pain management.

As an example, a new study funded in the past year is examining the experiences of 250 older persons with advanced dementia during the end-stages of their disease and dying process, in the nursing home setting, about which there exists very little information. The goals of the CASCADE study - Choices, Attitudes, and Strategies for Care of Advanced Dementia at the End-of-Life - are to describe disease trajectory and clinical course; identify modifiable aspects of care associated with greater resident comfort, including during the dying process; and repeatedly assess substitute decision-maker (SDM) satisfaction with decision-making. As the first comprehensive, rigorous prospective investigation of nursing home residents with advanced dementia and their families, this study is designed to promote the understanding of patient suffering, prognoses, decision-making, and family burden in this population near the end-of-life.

A recent training award is to further career development and research that will inform and improve palliative care for older adults with chronic critical illness. The overall goals of this research training project are to assess palliative care needs of chronically critically ill older adults, including pain; evaluate the influence of unmet palliative needs on important clinical outcomes of chronic critical illness; and test targeted interventions to improve palliative care and associated outcomes of older adults with chronic critical illness.

Other recently funded studies in the wide-ranging NIA portfolio are examining the course and consequences of musculoskeletal pain in an older population; the effects of aging on brain responses to painful stimuli; the effects of age, race, and socioeconomic status on the ability to cope with arthritis; and the impact of pain on physical functioning in the elderly.

Item

Parkinson's disease – The Committee encourages NIA to collaborate with NINDS in developing a greater understanding of the overlap in benefits that current research could provide to understanding both Alzheimer's and Parkinson's disease. The Committee applauds the significant investment by NIA in understanding the role of genes, including alpha-synuclein, in the causation and manifestation of Parkinson's. Work of this nature is critical for better comprehension of the disease process,

identification of potential pharmaceutical agents, improved diagnostic ability, especially during the nearly stages of the disease, and the development of accurate animal models. (p. 91)

Action taken or to be taken

The NIA continues to collaborate with the NINDS, the NINDS Udall Centers, and the Alzheimer's disease Research Centers (ADRCs) to foster utilization of resources to study clinicopathological correlations and basic science in a range of neurodegenerative diseases, including Parkinson's disease (PD) and Lewy Body dementia. NIA staff participates in the NIH PD Coordinating Committee, and NIA is part of the Deep Brain Stimulation Consortium.

Several promising PD studies, some in response to FY2004 initiatives, are being supported by NIA. One project will be doing a genomic and genetic analysis of a drosophila transgenic that replicates the features of PD including age-dependent, progressive degeneration of dopaminergic neurons and movement disorder. Another will investigate biomarkers of PD that are present in human brain, and ventricular and spinal cerebrospinal fluid; a high throughput proteomic approach will be used to identify proteins unique to PD, PD progression, and development of cognitive deficits in PD.

Orolingual motor deficits – intermittent facial movements, initially involving the tongue and lips - are present in PD, and may be related to associated eating and swallowing dysfunction. One project has been examining the relationships between aging, orolingual motor function and the dopamine pathway in rats. Little is known about the mechanism of this motor function and this work represents a novel approach using an animal model.

Another innovative project will use the atomic force microscope to provide quantitative information on the magnitude of interactions between alpha-synuclein and lipids to determine the role of protein-lipid bilayer interactions in alpha-synculein aggregation.

A recent meeting, co-sponsored by the NIA and NINDS, on the overlap of Parkinson's Dementia (PDD), Dementia with Lewy bodies (DLB) and Alzheimer's disease (AD) resulted in a series of recommendations, including the establishment of workgroups with representation from both the Alzheimer's Centers and the Udall Centers. These groups will address research issues such as assessment of the non-motor features in the dementias occurring in PDD, DLB and AD including visuo-spatial difficulties, fluctuating cognition, sleep disturbances and autonomic disturbances. Other groups will address neuropathological and biochemical profiling of the three dementias, family studies of PDD and LBD along with harmonization with family studies in AD, and identification of biomarkers and treatment targets for the three overlapping dementias.

FY 2005 Senate Appropriations Committee Report Language (S. Rpt. 108-345)

Item

Alzheimer's Disease –. . . . .Alzheimer's is also having a corrosive effect in the private sector, costing U.S. businesses $61,000,000,000 in 2002, an amount equivalent to the net profits of the top 10 Fortune 500 companies. The Committee notes, however, that rapid advances in basic science are helping to identify multiple targets for therapies that may help slow or halt the progression of Alzheimer's disease.

Before these promising advances can be put to use preventing or treating the disease, they must be tested and validated in controlled clinical trials. Given the tremendous toll Alzheimer's disease exacts in human suffering, health care costs and economic loss, the Committee strongly urges NIA to launch simultaneous clinical trials on therapies it determines to be most promising. The Committee also encourages NIA to work collaboratively with other institutes and the CDC to educate Americans about the ways they can maintain their brain as they age. (p. 135)

Action taken or to be taken

Please refer to pages 31 of this document for NIA's response to this significant item regarding Alzheimer's disease.

Item

Alzheimer's Research Caregiver, Education, and Training – The Committee recommends that the NIA establish cooperative working relationships with non-profit organizations dedicated to new approaches to care-giving for patients with Alzheimer's disease, and to expand the level of resources made available for Alzheimer's disease caregiver education, research, and training. (p. 136)

Action taken or to be taken

The NIA has extensive cooperative working relationships with a variety of Alzheimer's disease (AD) and Caregiving Groups including the Alzheimer's Association, Alzheimer's Foundation of America, National Family Caregiver Alliance, Family Caregivers Association, John Douglas French Alzheimer's Association, American Health Assistance Foundation, and the Leeza Gibbons Memory Foundation and Leeza's Place. The NIA also has strong connections with its network of AD Centers (ADCs) and shares findings in caregiver research with these organizations and with individual caregivers. Many of the groups have connections with the nearest ADC, and caregivers participate in research at the ADCs.

A series of caregiver pamphlets is provided free of charge to individuals and to the aforementioned organizations. They are available in English and in Spanish and include materials that have been developed through the ADC programs. Caregiver research funded by NIA has been highlighted in the most recent AD Progress Report, which is being mailed to these organizations, and additional copies are available to these groups to distribute through their own channels.

The NIA has an extensive program of both basic and applied research on caregiving. Recent projects have included a study showing that caregivers are at risk for adverse health outcomes even after their patient has been institutionalized, and a randomized controlled trial showing multiple benefits from exercise plus behavioral management for AD patients. NIA-funded research has demonstrated the utility of computer-based caregiving information and telephone reminders for caregivers to exercise. The NIA-funded Health and Retirement Study conducted a conference on "Older Families" in 2004, bringing together an interdisciplinary group of researchers working on topics such as parent care and stress, allocation of elder care responsibilities within families, and transitions to nursing homes.

The NIA and the National Institute on Nursing Research sponsor the Resources for Alzheimer's Caregiver Health (REACH) program of interventions to improve the health and well-being of dementia

caregivers. The first phase of REACH was designed to test feasibility of interventions; REACH II, now in progress, is examining the effectiveness of interventions incorporating the more successful elements of first phase trials. REACH includes training in caregiving skills and tailored coping strategies. Related research on how caregivers in different racial and ethnic groups differ in their perceived stress and rewards of the caregiving role, their use of formal in-home assistance, and in religious coping and participation is ongoing.

Item

Behavioral Research and Older Workers – The Committee encourages NIA to expand research on the needs of older workers. Since more baby boomers will be working well beyond the traditional age of retirement, more information is needed about the ways in which workplaces and workplace technology can be better designed to accommodate the needs of older workers. (p. 136)

Action taken or to be taken

The NIA co-sponsored a National Research Council (NRC) / Institute of Medicine report on "Health and Safety Needs of Older Workers," and sponsored an NRC report on "Technology for Adaptive Aging." These reports, both published in 2004, are expected to guide further behavioral research on older workers.

NIA interest in work and aging is shown by continued funding of the Center for Research and Education for Technology (CREATE), with projects focused on the usability of technology by older individuals and on the potential for technology to support internet-based jobs for older individuals. NIA commissioned three review papers in 2004 on functional measures of work capacity, work complexity and cognitive function, and work, cognitive capacity and interaction with technological advances. An exploratory workshop focused on these issues is planned for summer 2005. Through an Intra-Agency Agreement, NIA also supports intramural research on the relationship between work complexity, work self-direction, and cognitive function in older populations.

The NIA is interested in research on work exposures, and the psychosocial and physical demands of a broad range of occupations to develop better estimates of the functional demands and benefits of those occupations. Research on the social and economic costs of workplace disease and injury also fits with NIA interests in the older worker.

The NIA research portfolio and data collection also support this agenda by providing information on trends in work and retirement behavior and expectations, and their relations to health problems. NIA funds the Heath and Retirement Survey and aging supplements to the Panel Study of Income Dynamics, both cited in "Health and Safety Needs of Older Workers" report as important data sources for assessing and forecasting needs.

Item

Bone Diseases – The Committee encourages NIA to increase research into the pathophysiology of osteoporosis, Paget's disease and osteogenesis imperfecta. This research should include: genetics, the role of cell aging and altered metabolism, environmental and lifestyle factors, bone responsiveness to

weight bearing, bone quality and fracture incidence, bone marrow changes, new agents to increase bone mass, the therapeutic use of new technology, and the comorbidity of metabolic bone diseases with chronic diseases of aging. (p. 136)

Action taken or to be taken

The NIA supports a broad range of research on bone diseases related to aging, including research on hormonal changes, cellular changes, genetics, lifestyle factors, weight bearing and agents to increase bone mass. The NIA has an ongoing Program Announcement (PA), with NIAMS and NICHD, on "Aging Musculoskeletal and Skin Extracellular Matrix." This PA was issued to stimulate research applications on age-related changes in bone matrix and on alterations in matrix with age-associated diseases such as Paget's disease, as well as research on how alterations in activity levels or function affect matrix structure and function in the context of disabling conditions, which could include muscle atrophy, osteoporosis or osteogenesis imperfecta.

Several important results concerning bone mass have been reported recently. Novel studies have shown for the first time that thyroid stimulating hormone (TSH), the body's regulator of thyroid activity, also has direct effects on bone turnover activity. This not only helps explain low bone mass (osteopenia) associated with hyperthyroidism (in which patients have very low levels of TSH), but opens an entirely new direction in investigations of bone regulation. In another study, bone was shown to be a target for the antidiabetic compound Rosiglitazone, which is used to treat type 2 diabetes, a common condition in the elderly. However, it also appears to pose a significant risk to skeletal health and may act to increase the tendency for marrow cells to form fat instead of build bone. In aging bone, the phenomenon of fat formation by cellular progenitors for bone and muscle may be one factor leading to imbalance of bone-building versus bone-destroying cells and consequent osteopenia. Investigation of key factors leading to formation of fat cells in aging musculoskeletal tissues and the effects on bone mass and muscle health, as well as effects on metabolism and overall health, are areas of NIA research interest.

Peak bone mineral density (BMD) appears to be a major determinant of risk of developing osteopenia and osteoporosis and has a large genetic component. Studies this year confirmed that peak BMD at the hip is linked to genetic loci on two chromosomes, and that peak BMD in vertebrae is linked to another chromosome. The vertebral locus corresponds to a similar chromosomal region that determines peak BMD in mice, and studies are ongoing to identify the specific genes involved. NIA is planning an initiative that will use existing data and specimens from other studies to identify factors that maintain BMD in older women as they age.

Although osteoporosis is often thought of as a disease of women, because they become particularly susceptible at menopause, it also affects high numbers of men. The estrogen receptor is known to be important in this process, and studies have now shown that men with higher levels of estradiol have higher BMD, and that specific genetic variations in the subtypes of estrogen receptor can modulate BMD. Additional studies in men characterized bone loss with age and potentially modifiable characteristics - increasing age, low body mass, weight loss, smoking and physical inactivity were all associated with bone loss in men.

Item

Claude D. Pepper Older American Independence Centers – The Committee continues to strongly support these successful centers, which focus on developing innovative and cost-effective ways to enhance the independence of older Americans. The centers also play a critical role in developing top-level experts in geriatrics. The Committee again urges NIA to make all possible efforts to expand these centers to include a school of nursing. (p. 136)

Action taken or to be taken

The NIA continues to value this important program, for which three meritorious applications were funded in FY 2004. The most recently reviewed applications were in response to the RFA for Claude D. Pepper Older Americans Independence Centers (OAICs), which was open to schools of nursing along with other institutions. Nursing faculty continue to be intimately involved in OAIC research, making important contributions to better our understanding of interventions to improve and maintain health and function among older persons. One of the currently funded OAICs is directed by a nurse with a faculty appointment in the school of nursing at the institution, and NIA will continue to welcome applications from schools of nursing for inclusion in the Claude D. Pepper Older American Independence Centers Program.

Item

Cognitive Research – The Committee has noted the results of the NIA-funded clinical trial, ACTIV, in which interventions to improve various aspects of cognition in older people were found to be effective, but did not generalize to improved cognitive performance overall. Understanding that changes in memory and cognition are troubling to older people and threaten their independence, the Committee encourages NIA to consider next steps in research to develop cognition-enhancing interventions and report back on additional efforts. (p. 136)

Action taken or to be taken

Cognitive changes associated with increased age can become as great a disability as physical changes. NIA is interested in programs designed to intervene, slow-down, and reduce disability in these areas. This significant interest and investment in cognitive interventions is evidenced by the Advanced Cognitive Training for Independent and Vital Elderly (ACTIVE trial) -now in Phase II follow-up to the Phase I clinical trial intervention - that developed training for speed, memory, and reasoning. The training intervention was successful in raising performance, but the ultimate goal of assessing impact on instrumental activities of daily living requires further analysis of the degree to which cognitive training in specific domains can have an impact on disability, in domains that require a broad range of cognitive function. Preliminary results from ACTIVE suggest that conditions such as hypertension and diabetes do not influence the response to training, although individuals with those conditions start from lower levels. New results from the analysis of the ACTIVE trial suggest that training-related improvements in visual processing speed can improve attention, as it relates to driving and reduced crash risk.

Several other grants from NIA focus on cognitive intervention, including interventions involving self-monitoring of cognitive strategies; the Center for Translational Research on Aging and Mobility with a

focus on driving, and the Center for Healthy Minds with a focus on social interaction as a context for cognitive intervention.

The NIA sponsored a Symposium on "Cognitive Training for Older Adults" in March 2004, which gathered 11 leading cognitive researchers to address: 1) the state of the art in development of cognitive interventions and are we ready to turn research findings into practice; 2) key research and methodological issues that the consumer, practitioner, and the researcher should be aware of when embracing the concept of cognitive intervention; and 3) how to judge the success of a cognitive intervention. Participants suggested that multilevel cognitive interventions involving exercise, social engagement, lifestyle management, and the combination of training and medications will be most promising. Articles from this symposium are to be published in a special issue on cognitive training and intervention in the *Journal of Gerontology*. A Program Announcement will be developed to encourage the development of new, innovative, and theoretically driven approaches to cognitive intervention programs.

Item

Demographic and Economic Research – The Committee once again commends the NIA for supporting demographic and economic research and, in particular, the NIA Demography of Aging Centers program. Since its inception 10 years ago, the program has supported invaluable research to enhance knowledge about the well being of older Americans – especially information about their health and socioeconomic status, including their income, savings, work, and retirement decisions. Researchers at these Centers have initiated critical surveys, such as the Health and Retirement Survey and the National Long-Term Care Survey, which have, for example, identified social and economic consequences of retirement and the decline in disability among older Americans, respectively. After a decade, the Centers are poised to make significant contributions on numerous policy issues confronting an aging society. The Demography Centers are also now in a unique position to collaborate with several of the NIA Roybal Centers program to help translate findings into interventions and improve quality of life for older people. Therefore, the Committee urges NIA to continue its strong support of the demography centers program. (p. 137)

Action taken or to be taken

In 2004, the NIA awarded multi-year grants for Centers on Demography of Aging to nine continuing centers and four new ones; four of the centers are co-funded by the NIH Office of Behavioral and Social Sciences Research. The centers foster multi-disciplinary research on an array of issues especially relevant to the well-being of older Americans as the oldest of the "Baby Boom" generation approach retirement. The Health and Retirement Study has added a new cohort, representative of the older Baby Boomers, to the current wave of data collection, and will provide information on crucial questions of how their savings, retirement, and health care decisions differ from those of previous generations. The Centers' research includes the age structure of populations; changes in the levels of disease and disability; the economic costs of disability; cost effectiveness of interventions; migration and geographic concentration of older people; decision-making about retirement; pensions and savings; the relationship between health and economic status; and health disparities by gender and race. A coordinating center will organize efforts to share research results widely and to involve researchers new to aging issues.

The National Long-Term Care Survey (NLTCS) went to the field in November 2004 for its sixth wave of data collection, and fieldwork is planned to be completed in February 2005. An NLTCS Conference was held in November 2004 in Washington, D.C. to present papers covering diverse topics and to introduce the NLTCS to a broader audience of researchers and policy makers. The NIA supports research following up on the NLTCS finding of declining disability at older ages, with studies of the specific causes and work on interventions to hasten disability decline. The six new Roybal Centers contribute in several ways to this effort, ranging from developing new tools for patient management and decision-making by older people to forecasting the effects of new technology on medical care and expenditures.

Item

Down Syndrome – Research has shown that all persons with Down syndrome develop the neuropathological findings of Alzheimer's disease, and that many go on in later life to show cognitive decline. The Committee strongly urges NIA to increase funding to study the connection between Alzheimer's disease and Down syndrome and to work closely with NINDS, NICHD, NIMH and NHGRI to establish a new, multi-year research initiative to fund Down syndrome research on improving cognition and preventing early dementia through biomedical treatments. (p. 137)

Action taken or to be taken

Please refer to pages 32 of this document for NIA's response to this significant item regarding Down syndrome.

Item

Hematology Research – The Committee remains interested in advancing research opportunities into blood disorders in the elderly population. The Committee is particularly concerned that the incidence and prevalence of anemia increases with age; after age 85, one quarter of the population is anemic. Research is needed to better understand the basic biology and adverse quality of life complications of anemia and other blood diseases in the elderly. The Committee is supportive of the ongoing collaboration between the American Society of Hematology and NIA, with the participation of NHLBI, NCI, and NIDDK, to develop a research agenda in this field. (p. 137)

Action taken or to be taken

Anemia is the most frequently encountered hematological problem in geriatric practice. Over half the cases of anemia in older adults are without an identifiable cause, so there is no therapeutic intervention directed at an underlying condition. Anemia in the elderly is associated with reduced survival and increased risk of functional decline, acute coronary events, cognitive impairment, and drug complications. Projects are seeking to identify the mechanisms involved in anemia in the elderly and the effectiveness of treatment with erythropoietin (EPO), and to understand the underlying causes of anemia associated with chronic diseases and inflammation.

The American Society of Hematology (ASH) has worked closely with NIA and other institutes to establish a research agenda on anemia in the elderly. An ASH workshop on the "Clinical Implications of

Anemia in the Elderly" was held in March 2004 to determine where gaps exist in current knowledge and to identify research opportunities and priorities; a report of this workshop will be published in the journal *Blood* in Spring 2005. Program staff from NIA, NHLBI, NCI and NIDDK participated in the ASH workshop and will work collaboratively to identify opportunities for initiatives to address research priorities within the missions of the institutes.

In October 2003, NIA issued two RFAs for stem cell research. Six of the funded applications explore hematopoietic (blood) stem cell (HSC) regulation and function in association with aging and aging-related conditions, and findings should begin to address the role of HSC dysfunction or responsiveness to EPO and changes in hematopoietic reserve associated with aging.

One likely cause of anemia in the elderly is early myelodysplasia, caused by the gradual accumulation of mutations in stem cells, which impairs their reproduction. The NHLBI has issued an RFA on "Myelodysplastic Syndrome (MDS): Seeking Cure Through Discovery on Pathogenesis and Disease Progression." This initiative is expected to lead to new approaches to disease detection, treatment, and prevention. The NCI is also interested in MDS, and staff had a planning meeting at the December 2004 ASH annual meeting to discuss possible formation of an MDS Consortium to do clinical trials.

Anemia of chronic inflammation (ACI) is one of the most common forms of anemia in the aged, and may be a major contributor to the reduction in red cell mass that often accompanies aging. Although EPO is used to treat this anemia, the precise role and indications for erythropoietin in ACI remain to be established. The NIDDK is planning a new initiative to determine the pathophysiology of ACI and the inflammatory and genetic factors involved, and to develop diagnostic standards and a definitive therapy for ACI.

Item

Parkinson's disease – The Committee encourages NIA to collaborate with NINDS in developing a greater understanding of the overlap in benefits that current research could provide to understanding both Alzheimer's and Parkinson's disease. The Committee applauds the significant investment by NIA in understanding the role of genes, including alpha-synuclein, in the causation and manifestation of Parkinson's. Work of this nature is critical for better comprehension of the disease process, identification of potential pharmaceutical agents, improved diagnostic ability, especially during the nearly stages of the disease, and the development of accurate animal models. (p. 137)

Action taken or to be taken

Please refer to pages 34 of this document for NIA's response to this significant item regarding Parkinson's disease.

NATIONAL INSTITUTES OF HEALTH
National Institute on Aging

Authorizing Legislation

	PHS Act/ Other Citation	U.S. Code Citation	2005 Amount Authorized	FY 2005 Appropriation	2006 Amount Authorized	2006 Budget Estimate
Research and Investigation	Section 301	42§241	Indefinite	$1,027,607,000	Indefinite	$1,032,820,000
National Institute on Aging	Section 443	42§285e	Indefinite		Indefinite	
National Research Service Awards	Section 487(D)	42§288	a/	24,383,000	b/	24,383,000
Total, Budget Authority				1,051,990,000		1,057,203,000

a/ Amounts authorized by Section 301 and Title IV of the Public Health Act.

b/ Reauthorizing legislation will be submitted.

NATIONAL INSTITUTES OF HEALTH
National Institute on Aging

Appropriations History

Fiscal Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation 1/
1997	$461,541,000 2/	$484,375,000	$470,256,000	$484,806,000 3/
1998	495,202,000 2/	509,811,000	520,705,000	$519,279,000
1999	554,391,000 2/4/	565,574,000	596,521,000	596,521,000
Rescission				(395,000)
2000	612,599,000 2/	651,665,000	680,332,000	690,156,000
Rescission				(3,667,000)
2001	721,651,000 2/	790,299,000	794,625,000	786,039,000
Rescission				(285,000)
2002	879,961,000	873,186,000	909,174,000	893,443,000
Rescission				(313,000)
2003	958,155,000	958,155,000	1,000,099,000	1,000,099,000
Rescission				(6,501,000)
2004	994,411,000	994,411,000	1,031,411,000	1,024,598,000
Rescission				(6,557,000)
2005	1,055,666,000	1,055,666,000	1,094,500,000	1,060,666,000
Rescission				(8,676,000)
2006	1,057,203,000			

1/ Reflects enacted supplementals, rescissions, and reappropriations.
2/ Excludes funds for HIV/AIDS research activities consolidated in the NIH Office of AIDS Research.
3/ Excludes enacted administrative reductions of $241,000.
4/ Reflects a decrease of $1,679,000 for the budget amendment for bioterrorism.

NATIONAL INSTITUTES OF HEALTH
National Institute on Aging

Detail of Full-Time Equivalent Employment (FTEs)

OFFICE/DIVISION	FY 2004 Actual	FY 2005 Appropriation	FY 2006 Estimate
Office of the Director	25	25	25
Intramural Research Program	261	261	261
Office of Administrative Management	25	25	25
Office of Extramural Affairs	20	22	22
Biology of Aging Program	12	12	12
Geriatrics & Clinical Gerontology Progra	8	8	8
Behavioral & Social Research Program	10	11	11
Neuroscience & Neuropsychology of Aging Program	15	15	15
Total	376	379	379
FTEs supported by funds from Cooperative Research and Development Agreements	(0)	(0)	(0)

FISCAL YEAR	Average GM/GS Grade
2002	10.5
2003	10.7
2004	10.9
2005	10.9
2006	10.9

NATIONAL INSTITUTES OF HEALTH
National Institute on Aging

Detail of Positions

GRADE	FY 2004 Actual	FY 2005 Appropriation	FY 2006 Estimate
Total - ES Positions	4	4	4
Total - ES Salary	$578,196	$598,432	$612,196
GM/GS-15	29	29	29
GM/GS-14	28	28	28
GM/GS-13	28	28	28
GS-12	63	63	63
GS-11	46	46	46
GS-10	2	2	2
GS-9	26	26	26
GS-8	21	21	21
GS-7	24	24	24
GS-6	13	13	13
GS-5	5	5	5
GS-4	0	0	0
GS-3	0	0	0
GS-2	0	0	0
GS-1	0	0	0
Subtotal	285	285	285
Grades established by Act of July 1, 1944 (42 U.S.C. 207):			
Assistant Surgeon General	1	1	1
Director Grade	5	5	5
Senior Grade	0	0	0
Full Grade			
Senior Assistant Grade			
Assistant Grade			
Subtotal	6	6	6
Ungraded	91	91	91
Total permanent positions	0	0	0
Total positions, end of year	386	386	386
Total full-time equivalent (FTE) employment,end of year	376	379	379
Average ES salary	$144,549	$149,608	$153,049
Average GM/GS grade	10.9	10.9	10.9
Average GM/GS salary	$71,016	$73,502	$75,192