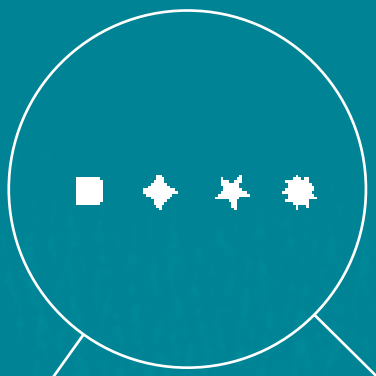
National Institutes of Health

National Institute on Aging

PORTFOLIO FOR PROGRESS



The mission of the National Institute on Aging: "the conduct and support of biomedical, social and behavioral research, training, health information dissemination, and other programs with respect to the aging process and the diseases and other special problems and needs of the aged."

Research on Aging Act of 1974,
as amended in 1990 by P.L101-557

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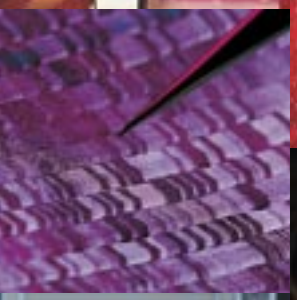
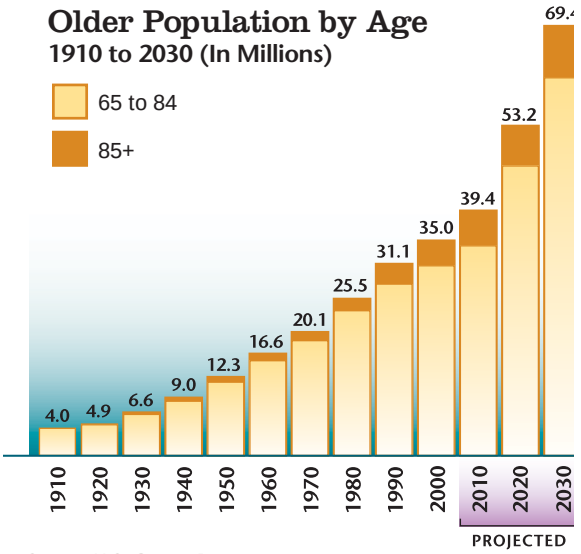




TABLE OF CONTENTS

Dr. Richard J. Hodes
Director, NIA



Source: U.S. Census Bureau

NEVER BEFORE HAVE SO MANY PEOPLE LIVED FOR SO LONG.

The trend toward very advanced age was remarkable in the 20th century and is expected to continue unabated until at least the middle of the new millennium. Only 10 million people reached age 50 or older in 1900, a time when the average life expectancy was only 49. Today, some 76 million of us are age 50 or more. A newborn can expect to live well into his or her seventies and very often beyond. Looking ahead, the first wave of the famous "baby boom" will turn 65 in 2011, accelerating an already underway "senior boom." We are captivated, too, by the notion that more and more of us will be centenarians.

This aging of America moves us into a new phase of our national life, with profound implications for individuals, families, and society. A portrait of an older America is beginning to emerge, and it is a conflicted one. On one hand, research finds that we are healthier and wealthier than ever before. A majority of us age 65 and older say our health is good or excellent. Rates of disability and of several diseases are falling dramatically, despite a notable increase in the number of older people. Fewer of us live in nursing homes than did just a decade ago. And the poverty that used to accompany advancing age has been greatly reduced.

On the other hand, however, good health and well-being with age are far from a universal reality. Studies show that most of us age 70 and older have at least one of seven potentially disabling conditions, such as arthritis, heart disease, or diabetes. About one-fifth of people 65 and older — seven million in all — report some level of disability. At greatest risk for disease and disability is the age group that is growing the fastest, people age 85 and older, nearly half of whom suffer from Alzheimer's disease (AD). Family and friends are often brought into the picture as caregivers, making up a large and informal corps of support for loved ones who cannot function well on their own.

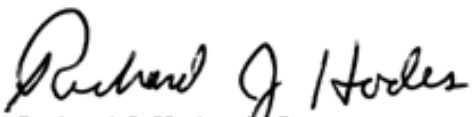
Understanding this dichotomy — between an independent, active later life and one that is

Dr. Judith A. Salerno
Deputy Director, NIA

characterized by frailty and dependence — is what research on aging is all about. Discovering what happens in the many, varied manifestations of aging, even in different species, will allow us to develop insights and interventions that promote health and prevent disease.

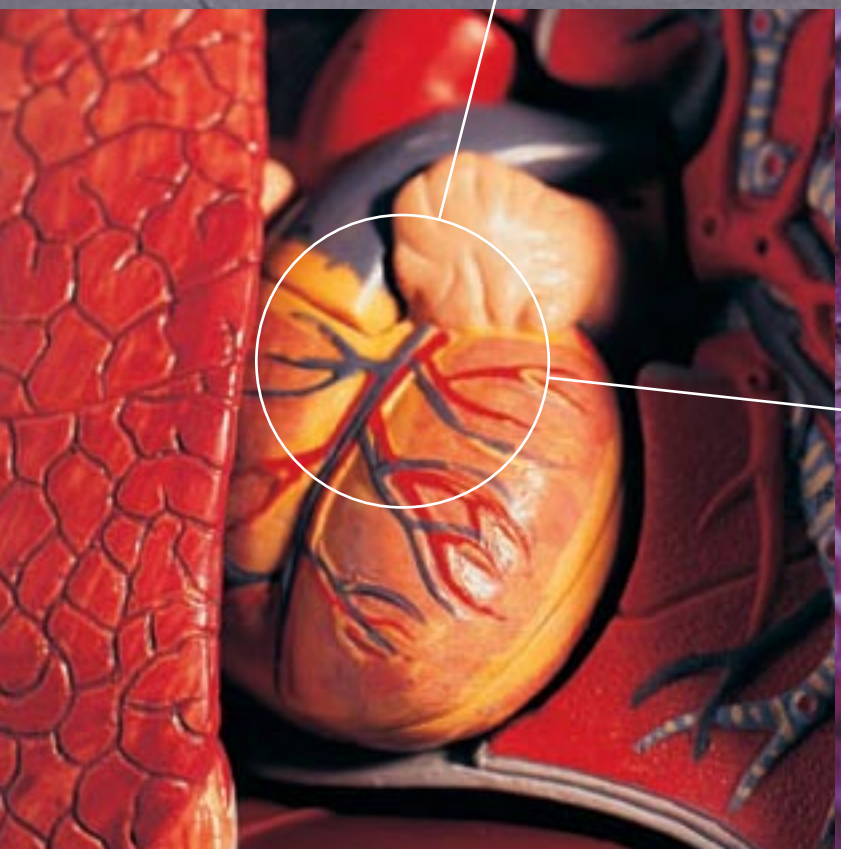
The research program pursued by the National Institute on Aging (NIA), part of the National Institutes of Health, covers a broad range of issues and concerns. Aimed at improving the quality of life for older people and their families, research is focused in four general areas — the biology of aging, reducing disease and disability, AD and cognitive changes, and the behavioral and social aspects of aging. Within this framework, scientists and those supported by Institute grants and contracts explore everything from cell function to social interaction. Overall, there is an increasing emphasis on the study of gender and racial and ethnic disparities in health and a concentrated effort to include more minorities in research and train new minority scientists.

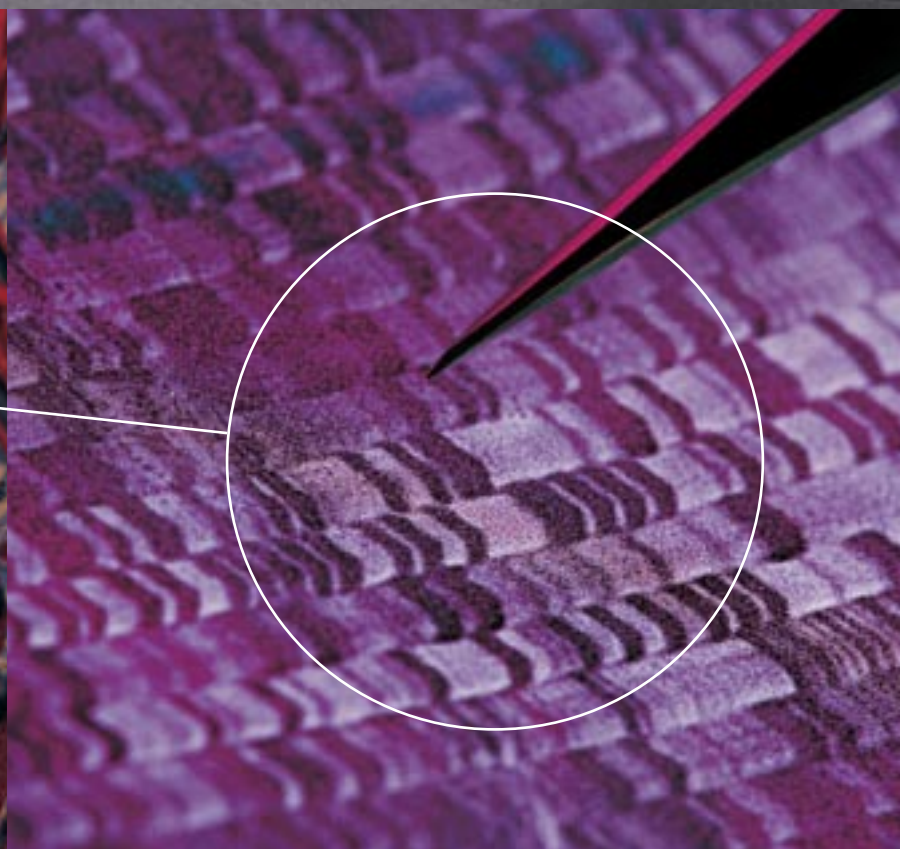
Enormous progress is being made. This booklet describes some of what we know and what we have yet to find out about growing older. Research has already contributed to the revolution in longevity. What we now seek are ways to embrace aging, individually and collectively, and make it the best that it can be.



Richard J. Hodes, M.D.
Director, National Institute on Aging

The Biology of Aging





The Biology of Aging

"Gee, he sure doesn't look 70." "Oh, she's got to be at least 60." "You're *how* old?"

At one time or another, most of us have formed some opinion about what it is to look or feel a certain age. The truth is, of course, there's no real standard. One 75 year-old may be active and healthy, with an almost visible vitality. Another can project a more stereotypical image of someone in his or her mid 70s, perhaps with a few wrinkles and a bit slower in step.

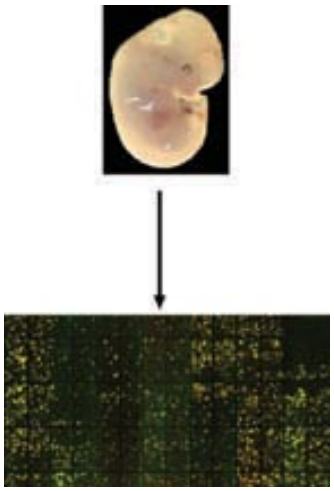
The basis for much of modern research on aging is this notion of heterogeneity, or differences, among individuals. That is, people "age" differently — outwardly, in the appearance of our hair, eyes, and skin, and inside, in our muscles, bones, heart, brain, and other vital tissues and organs. It is now clear to scientists that each of us is a product of a complex mix of heredity, environment, and lifestyle. Understanding the genetic, molecular, and cellular processes common to aging as well as how these processes may differ in individuals will lead to biological and lifestyle interventions that maintain function and prevent disease.

The past decade of study has moved us away from the idea that any one process or gene is responsible for how we age biologically. "There is no single theory to explain aging," says Dr. Huber Warner, NIA Associate Director, Biology of Aging Program. "It's possible that some age-related changes are genetically programmed while others involve the effects of less predictable activity, such as free radical damage to cells or other insults that seem to occur with age."

Research supported and conducted by the NIA examines many of these fundamental mechanisms of aging — in genes, in the biochemistry of cells, and in critical organs of the body. Scientists expect that the next few years will be particularly prolific for basic research on aging because of the promise of a number of new technologies. From the use of new microarray techniques to measure the activity of thousands of genes at once to refinements in developing new animal models for the study of gene function, "I think the development of technologies for a new generation of research at the genetic and molecular level will bring major breakthroughs in the biological sciences," says Dr. Warner.

Scientists at the NIA's Laboratory of Genetics, for example, have taken a major step forward in the use of new microarray technologies. The laboratory's work is based on the thinking that important genes begin to determine the course of aging at the very start of life. But these studies have lagged because many of the genes active in early life have not been part of gene libraries

AT ONE TIME OR ANOTHER, MOST OF US HAVE FORMED SOME OPINION ABOUT WHAT IT IS TO LOOK OR FEEL A CERTAIN AGE.



At the top is the mouse embryo about two-thirds of the way through its development. Genes that are active in the embryo at this time are shown as the colored spots on the NIA 15K microarray.

previously made available for analysis. Senior investigators in the laboratory's Developmental Genomics and Aging Section recently developed a new method to recover copies of all the genes "expressed" — turned on and functioning — in the early stages of development of mouse embryos. They have so far recovered 15,000 unique genes and have made a clone set freely available to the research community worldwide for further study. "This important tool will help analyze changes in the expression of many genes during aging and/or during stress," says Dr. David Schlessinger, chief of the Laboratory of Genetics. NIA scientists are working to release an expanded unique set of 26,000 genes.

THE GENETICS OF LONGEVITY AND DISEASE

Much of our knowledge about genes and aging comes from the study of laboratory animals, organisms, and animal and human cells. While not a perfect imitation of people, animal models like fruit flies, mice, and nematodes (worms) and organisms like yeast, have short life spans that allow scientists to pursue two lines of inquiry — how genes influence aging and how aging, in turn, may affect genetic stability and the biochemistry of cells and systems.

Studies of *Caenorhabditis elegans* (*C. elegans*), a genetically simple roundworm subject to scientific scrutiny for several years, and *Drosophila melanogaster*, a fruit fly, have been especially productive. For example, the *C.elegans*' *age*-1 and *daf*-2 gene products appear to play a role in determining longevity. The *daf*-2 gene was first identified because it controls an alternative state in the worm's development, called dauer formation. This state occurs during a stress, such as food scarcity or heat, when the worm responds by going into hibernation. A protein produced by the *daf*-2 gene moves the worm past this non-aging, dauer state when the stress is gone. Researchers have shown that when the *daf*-2 gene is altered so that the activity of the protein produced by the gene is reduced, the life span of the normal, fertile adult worm doubled. Mutations in some other *daf* genes have resulted in an increase in the worm's lifespan three or four times beyond its normal 2-week course. Similar results have been found in other yeast and fruit fly genes.

Drosophila melanogaster, a fruit fly

In order to gain insights that may prove valuable in the search for human longevity and disease-related genes, it is important to know if the genes found in animal models are like those found in mammals, including humans. The longevity genes found in *C. elegans*, for example, have striking similarities to genes found in fruit flies, mice, and

humans. Recent studies have shown that some of these longevity genes appear to affect the worm's nutrient-sensing pathway. Scientists believe that a further look into the similarities between the protein produced by the *daf*-2 gene and a human insulin receptor may advance understanding of how human insulin regulates metabolism and why this regulation fails in diabetes, and may even affect life span.

Another way scientists look at genetic influences on aging is to examine cases in which people exhibit exceptional longevity, either living to very advanced age or aging prematurely. In one study, NIA-supported scientists looked at 137 sets of brothers and sisters 90 years and older, with at least one sibling 98 and older, seeking to identify genes that may be linked to their longevity. A preliminary report from their genomic "scan" suggests that somewhere among the hundreds of genes in a region on chromosome 4 there could be a gene or genes whose subtle modifications influence aging and can give a person a better chance of living well beyond the average life expectancy. It may be, the researchers theorize, that some genes associated with human longevity could be involved in helping people avoid certain age-associated diseases.

Studies of premature aging have identified a defect in the WRN gene believed to be responsible for Werner's syndrome (WS), a disease in which people at a young chronological age develop some characteristics associated with aging, such as wrinkled skin, gray hair, cataracts, diabetes, heart disease, and osteoporosis. People with WS mostly die by age 50. Because of the apparent acceleration of aging in WS, scientists at NIA and at a number of laboratories supported by the Institute are delving into its causes, hoping to shed light on the disease and the degenerative processes that occur with normal aging. At NIA's Laboratory of Molecular Gerontology, scientists are focusing in on the high level of genetic instability in WS cells in an attempt to understand the abnormal nature of biochemical processes that are associated with this syndrome and develop during aging.

Werner's syndrome patient, age 14…

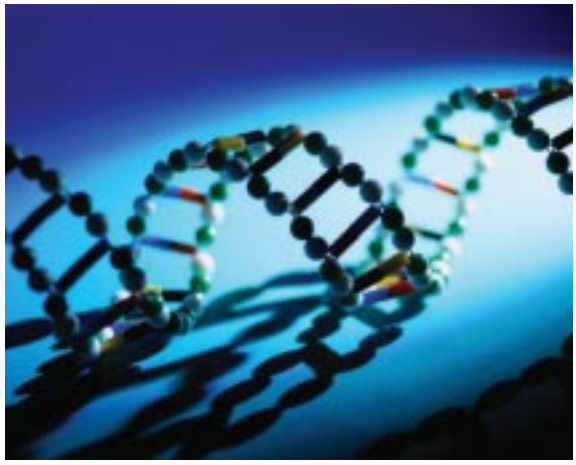
…and at age 48.

An NIA Laboratory of Genetics research team is studying the condition of premature ovarian failure (POF), in which a genetic mutation appears to both produce eyelid defects in newborns and trigger early onset of menopause decades later affecting the ability to bear children in women suffering with POF. The condition is an example of a critical process during aging that had been little investigated. The laboratory recently isolated a gene, FOXL2, required both for normal eyelid development and for formation of the full complement of eggs in the ovaries before birth. Continuing study of premature ovarian failure could help tell us how genetic processes during fetal development can affect aging later on. "It's becoming increasingly clear that early events in embryonic and fetal life are important for what happens later during aging," says Dr. Schlessinger. Having identified the gene and its purpose, the next phase of research is to look for underlying mechanisms that cause women with the mutation to produce fewer eggs and have an early menopause.

There may be other genetic differences that affect aging but are not as specifically damaging as mutations that cause conditions like POF. Scientific interest is increasing in

MUCH OF OUR KNOWLEDGE ABOUT GENES AND AGING COMES FROM THE STUDY OF LABORATORY ANIMALS, ORGANISMS, AND ANIMAL AND HUMAN CELLS.

OF PARTICULAR INTEREST IS DAMAGE TO CELLULAR MACROMOLECULES AND THE ENZYMES THAT PREVENT OR REPAIR IT.



single nucleotide polymorphisms, or SNPs, slight genetic differences in DNA that can be widespread in populations. SNPs occur in DNA in relatively high frequency in people, about one per every thousand base pairs. The effect of the differences may be slight, but over many years, they could contribute to the development of age-related declines and disease. An important goal of research is to identify these SNPs and determine which have a significant impact on aging.

How do the dozens, perhaps hundreds, of disease and longevity-related genes in humans exert their influence? One possibility is genetic control over cell division. Most cells have a finite life span; that is, after a certain number of divisions, they enter a state where they can no longer divide. Their ability to synthesize DNA is blocked and they fail to function appropriately. This "replicative senescence," as it is called, may help explain some aspects of the aging process. Several genes have been identified that seem to control senescence, some by triggering cell division and others that counter, or "silence," it.

Research into what causes cells to mature and to lose the capacity to reproduce promises to provide valuable insights about the causes of disease and disability. Digging even deeper into replicative senescence, for example, scientists have found cell division is accompanied by a reduction in the length of telomeres, the tail-like formations at the end of chromosomes, which shorten each time a cell divides. The telomeres protect the chromosomes, but can become so short that the chromosomes they are attached to can no longer replicate. One study found that mutant mice which undergo excessive telomere shortening in certain cells exhibit graying fur and fur loss, increased vulnerability to skin lesions and problems in wound healing. In addition, these mice were smaller and had a life span that was only 75 percent of normal.

ENVIRONMENTAL FACTORS AND AGING

When a gene is expressed, it produces a protein, which may be an enzyme, an antibody, a hormone, or one of tens of thousands of other proteins essential to the body. Some of these are believed to be linked to the aging process and have sparked a growing body of research on the molecular aspects of aging. Of particular interest is damage to cellular macromolecules — cell membranes, proteins, and DNA — and the enzymes that prevent or repair that damage.

Prime culprits in this damage are oxygen free radicals, highly reactive oxygen molecules that are products of normal metabolism of the mitochondria, the part of the cell that metabolizes sugars into energy. These free radicals can readily enter into chemical combinations, causing oxidative stress that can damage macromolecules. One defense against free radicals includes the body's manufacture of

antioxidants, which can neutralize the oxygen radicals, rendering them harmless. But studies in animals have not yet demonstrated directly that use of natural antioxidants, such as vitamin E, can improve health or extend life span.

There may be other ways to combat oxidative stress, and scientists are looking in some new directions. To date, laboratories have had mixed success in affecting the aging of animals genetically altered to "overexpress" either superoxide dismutase (SOD), or SOD and catalase, enzymes that reduce oxidative damage. One recent study in nematodes, however, not only provides evidence that oxidative stress is a major risk factor in the rate of aging, but strongly suggests that aging might be slowed and life span increased by a specific drug intervention. In this experiment, an artificial compound developed in the private sector, EUK-134, which mimics both SOD and catalase activity, was shown to increase the life span of nematodes by about 50 percent. EUK-134 also reversed premature aging in a strain of the worm with elevated oxidative damage. Perhaps this or similar compounds eventually could be developed to lessen oxidative stress in humans and delay or reduce some age-related diseases.

Of increasing interest is the effect of blood sugar — glucose — on health. "I think we are only just starting to learn the extent to which glucose metabolism affects the health and function of cells and tissues," Dr. Warner notes. Oxidative stress and cellular deterioration can be promoted by glucose in several different ways. In one process, glucose molecules, in an activity called non-enzymatic glycosylation or glycation, can bind themselves to proteins, and, after some molecular rearrangement, cause the proteins to hook together, or crosslink. Immune cells called macrophages can combat glycation. But scientists are discovering that this process is incomplete and that the crosslinked proteins, known as advanced glycosylation end products, or AGEs, accumulate with age. Appearing to toughen or stiffen tissues, AGEs are believed to be involved in several age-associated conditions such as atherosclerosis, cataracts, and reduced kidney function. The study of crosslinking is a particular focus of research on diabetes as well, a disease in which complications mimic physiologic changes that can accompany advancing age.

NEW COMPOUNDS MAY BE DEVELOPED TO LESSEN OXIDATIVE STRESS AND DELAY OR REDUCE SOME AGE-RELATED DISEASES.

VITAL SYSTEMS AND ORGANS

One way to directly focus on potential interventions against disease and disability is to look at the biological changes with age in tissues, vital organs, or particular body systems. This expanding area of study has uncovered a number of clues about the state of our heart, brain, kidneys, and other important systems with age. An especially active area of research is the musculoskeletal system — bone, cartilage, and muscle — as scientists look for ways to prevent frailty caused by diseases such as osteoporosis, osteoarthritis, or sarcopenia, the wasting away of muscle with age.

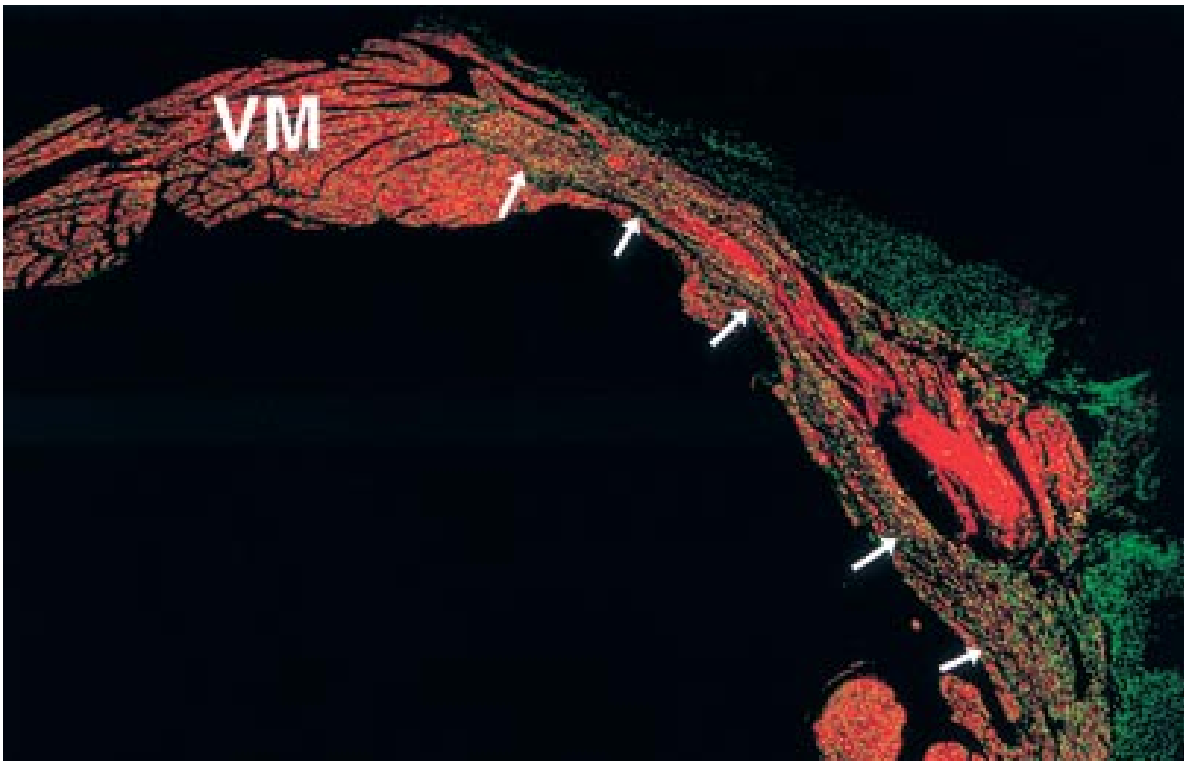
THE STUDY OF BIOLOGICAL CHANGES WITH AGE IN TISSUES, ORGANS, AND SPECIFIC BODY SYSTEMS MAY LEAD TO NEW INTERVENTIONS.

The biology of bone has been studied with increasing intensity in recent years, revealing possible new ways to treat and cure osteoporosis, an often crippling disease of bone loss and breakage. Ever since the discovery in the mid-1960s that bone is a dynamic tissue that constantly remodels, research has concentrated on the dynamics of the bone renewal process, particularly on the balance and regulation of bone degradation by cells called osteoclasts versus bone formation by other cells known as osteoblasts.

A major risk factor in osteoporosis is the loss of estrogen production in women at menopause and a consequent imbalance between bone-building cells and bone-destroying cells. After several years of research, one study team supported by NIA recently described a new action of estrogen. Instead of binding to estrogen receptors inside cells, where genes are housed, the scientists found that estrogen can act more quickly to attach itself to a receptor at the outer cell membrane. This new pathway, discovered in a cell culture, is the one that estrogen uses to extend the life of bone-building cells. The finding has implications for understanding the action of estrogen not only in bone, but in other tissues, including the heart and the brain. Further, it suggests that estrogen-mimicking drugs might be designed to lessen bone-thinning problems by rescuing bone-building cells from cell death.

Research on stem cells is another promising area of study for cell replacement or repair of specific tissues. It is hoped that these cells, which maintain the flexibility to "differentiate" from multi-potent cells into cells with specific functions, can be used in degenerative diseases where loss of cells is currently irreversible, such as musculoskeletal disorders, Alzheimer's and Parkinson's disease, stroke, heart attacks, immune system dysfunction, and diabetes. Several studies have suggested the potential for stem cell replacement therapy.

Recently, NIA-supported scientists examined cells from adult mouse bone marrow. In one study, the mouse marrow cells, when injected into the circulatory system of mice,



Regeneration of the infarcted heart in mice injected with hematopoietic stem cells. Arrows indicate newly formed myocardium in the infarcted region of the ventricular wall (VM is viable myocardium). Another study showed that adult mouse bone marrow cells could develop into neuronal (brain) cells.

found their way into the brains of the mice and within 1 to 6 months became neuronal cells. A second study showed that adult mouse bone marrow cells could also develop into heart cells and vascular structures, resulting in the substantial replacement of damaged heart tissue within 2 weeks.

A great deal of progress is being made in discovering the secrets of our aging cells and selves. But many scientists conducting research in this area sound a note of caution, as so-called "anti-aging" therapies are introduced into the marketplace. While some of these products and approaches may be based on sound theoretical or experimental concepts, many have not been tested adequately in large numbers of people for their ability to improve function and to measure potential side effects. Scientists are seeking, but do not yet have, despite considerable research, biomarkers, or measurements, of aging that could gauge the rate of aging or predict remaining years of life.

Concerned about possible growing use of these therapies, the NIA developed public information materials to outline what is known and what is not yet known about some of the more widely used hormones, vitamins, and other supplements marketed as antidotes to the effects of aging. NIA's television public service announcement on the subject, produced in 1999, garnered an Emmy award from the National Academy of Television Arts and Sciences, a first for a Federal Government agency. Its consumer publication, *Pills, Patches, and Shots: Can Hormones Prevent Aging?* is also widely distributed and may be obtained from the NIA Information Center or viewed online. See resources at the end of this booklet.

MANY SCIENTISTS SOUND A NOTE OF CAUTION AS SO-CALLED "ANTI-AGING" THERAPIES ARE INTRODUCED INTO THE MARKETPLACE.

Reducing Disease & Disability

Reducing Disease & Disability

The paramount goal of research on aging is to "add life to years," to use an expression favored by gerontologists and other experts on aging. Many of us will live far beyond the standard retirement marker of age 65, and we want our advanced years to be as active and healthy as they can be. Clinically-focused research at NIA looks for specific, practical ways to reduce disability and to promote independence by studying the causes, prevention, and treatment of health problems that occur as we age.

At one time, this interventionist view was not well understood, says geriatrician Dr. Evan Hadley, NIA Associate Director, Geriatrics Program. Dr. Hadley came to the NIA in the late 1970s, just a few years after the Institute's founding in 1974. He was among a new generation of physicians specializing in aging research and he recalls how disease and disability were widely thought to be inevitable consequences of aging. "I remember that many people were surprised by early studies showing that strength in the very old, even in people who were in their nineties, improved dramatically after strength training exercises," he notes.

Attitudes are only now beginning to change. "We still see, although perhaps less so, the old stereotypes that aches and pains and functional decline are 'just aging' and that nothing can be done about them. That's just not so. We now have powerful evidence that we can intervene for the better," says Dr. Hadley.

Chronic diseases and conditions like diabetes, cardiovascular disease, osteoporosis, and arthritis are major causes of frailty and disability in late life. Risks for disease and disability increase with age and can be made worse by our own lifestyle choices or by other behavioral and social factors. Scientists have come to believe, that, with age, certain changes in the body or the mind, such as hormonal or other shifts, could play a role in how we function in later life. While not characterized as disease, these "previously unappreciated" changes, as one NIA scientist calls them, can also affect cells or body systems in a way that leads to frailty or disability.

To investigate these diseases and age-associated changes, the NIA works closely with other parts of the National Institutes of Health, such as the National Cancer Institute (NCI); the National Heart, Lung, and Blood Institute; and the National Institute of Arthritis and Musculoskeletal and Skin Diseases. Research primarily funded and conducted by the NIA concentrates on the underlying causes of age-related disability and developing therapies for maintaining function with age. Cardiovascular disease, diabetes, and the maintenance of bone health and muscle function are of particular interest because of their impact on the daily lives of older people.

CLINICALLY-FOCUSED RESEARCH AT NIA LOOKS FOR SPECIFIC, PRACTICAL WAYS TO REDUCE DISABILITY AND TO PROMOTE INDEPENDENCE.

REDUCING CARDIOVASCULAR DISEASE

Cardiovascular disease (CVD) is the main cause of disability and the leading cause of death among people 65 and older. While we know a great deal about CVD and its risk factors, new areas of research are beginning to shed further light on the link between aging and the development and course of CVD.

Scientists at NIA are paying special attention to the relationship between vascular (blood vessel) aging and cardiac function. Studies by Dr. Edward Lakatta and investigators at NIA's intramural Laboratory of Cardiovascular Science (LCS) show that aging is accompanied by a thickening of the left ventricular muscular wall of the heart, affecting certain heart functions. Examining the mechanisms behind these changes, Dr. Lakatta, LCS Chief, and colleagues discovered that the culprit is vascular stiffness, a condition that occurs with age as flexible fibers in vascular tissue are replaced with less elastic collagen and calcium. This process heightens systolic blood pressure and pulse pressure and is associated with thickening of the interior layer of the blood vessel wall.

This arterial remodeling, once considered a "normal" part of aging, is really like a subclinical disease, in Dr. Lakatta's view, putting people at increased risk for cardiovascular disease with advancing age. In one recent epidemiological study, increased pulse pressure, which is determined to a substantial degree by large artery stiffness, was the best predictor of the risk of dying. "If vascular aging is a risk factor for disease, then it is a target for treatment and prevention," says Dr. Lakatta. "We are now turning our attention to ways to slow vascular aging down."

Researchers at NIA and elsewhere are testing a number of potential exercise and drug interventions for reducing arterial stiffness, with some success. In one approach, NIA and scientists at a private laboratory are looking at the compound ALT-711, a novel drug that breaks down vascular collagen bonds in the body. It alters the properties of the arterial wall by snipping bonds, or crosslinks, created in the arteries when glucose attaches to collagen. By altering the properties of the arterial wall, it is believed, the compound makes it easier for the heart to eject blood into the blood vessels. In studies of rhesus monkeys, 6 weeks after receiving the last treatment, all of the vessel walls tested were more flexible, and the effect persisted for more than 4 months after final administration of the drug. Blood flow through the heart also increased, an improvement that held for 10 months after the last treatment. Further research, including ongoing studies in people, is underway to confirm or extend these findings.

Other research in NIA's cardiovascular sciences laboratory seeks new ways to prevent

A Focus on Independence: The Claude D. Pepper Centers

Research at the Claude D. Pepper Older Americans Independence Centers targets one fear people have most about growing older—the decline of physical function and loss of independence. Created to organize and enhance research on aging, the Pepper Centers, as they are called, pursue a range of studies on aging. They also have a special mission to bring scientists from all disciplines into aging research and train the next generation of investigators in the field.

LIFE IS LIKE RIDING A BICYCLE. YOU DON'T FALL OFF UNLESS YOU STOP PEDDLING. — CLAUDE D. PEPPER

The Centers honor the memory of former Florida Senator and Congressman Pepper, whose legislative career was devoted to improving the lives of older Americans. The Pepper Centers conduct studies in the basic biomedical sciences, such as biology and genetics, as well as clinical and applied research that directly improves the lives of older people, and offer a unified structure in which scientists from different disciplines can contribute to each other's research. Research from a number of these Centers is cited throughout this booklet.

In 2001, the NIA supported nine Pepper Centers across the U.S., each with a specific area of emphasis beyond the basic role in research and training:

University of California at Los Angeles *(UCLA)* — Advance the understanding and practice of comprehensive geriatric assessment and examine ways to improve medical and nursing care for nursing home residents.

Duke University Medical Center, *Durham, NC* — Focus on improving the physical, psychological, and social functioning of older adults disabled by acute and chronic disease.

Harvard Medical School, *Boston, MA* — Develop junior faculty geriatricians into academic leaders, with a focus on innovative, multidisciplinary research and training in aging processes.

University of Maryland, *Baltimore* — Emphasis on cardiovascular disease. Study basic mechanisms and test aggressive approaches in diet, exercise, and smoking cessation to improve function with peripheral arterial disease.

Yale University Medical School, *New Haven, CT* — Use of a "multi-factorial" approach, looking at the combination of factors affecting functional ability and designing coordinated interventions to address them.

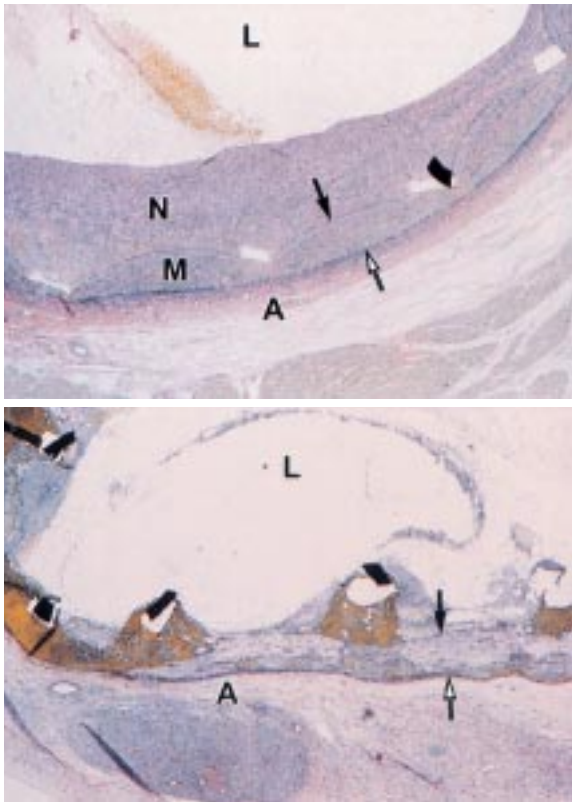
University of Texas Medical Branch, *Galveston* — Focus on basic mechanisms in cell biology and muscle function, aimed at interventions to maintain and improve muscle function.

Wake Forest University School of Medicine, *Winston-Salem, NC* — Use of behavior-based approaches, such as physical activity or nutrition, to hold off declines in physical function from diseases such as knee osteoarthritis.

University of Michigan, *Ann Arbor* — Foster collaboration and sponsor multidisciplinary research on cognitive and physical function, and health and well-being of older people looking at both basic mechanisms and interventions. Develop innovative projects to translate research findings into use and practice.

University of Kansas Medical Center, *Kansas City* — Emphasis on intervention studies for improving function of older people recovering from stroke, integrating this research with study of the underlying mechanisms of stroke recovery.

NEW AREAS OF RESEARCH ARE BEGINNING TO SHED FURTHER LIGHT ON THE LINK BETWEEN AGING AND THE DEVELOPMENT AND COURSE OF CARDIOVASCULAR DISEASE.



Paclitaxel-coated stent reduces restenosis following balloon angioplasty.

coronary artery restenosis. Restenosis is a gradual narrowing of the arteries that occurs as a consequence of vascular healing that follows angioplasty, the surgical procedure used to relieve arterial blockages by widening the vessels. Restenosis is aggravated by the implanting of stents, in which tiny metal scaffolds are placed inside the artery at the injury site to hold the vessel open. Restenosis usually occurs within 6 months of angioplasty and results from the migration of cells from the middle of the arterial wall into the inner layer of the artery, where they multiply and block normal blood flow.

Recognizing that cell division is crucial to the development of restenosis, scientists at the NIA and in laboratories elsewhere have begun to test the anti-cancer drug paclitaxel as a means of preventing the tissue growth that leads to vessel narrowing. Studies in laboratory animals demonstrate that coronary stents coated with paclitaxel can significantly delay restenosis, at lower doses and with less toxicity than the higher, anti-cancer doses of the drug. Clinical studies in Europe testing the approach developed in the NIA laboratory have been encouraging, and studies in the U.S. by NIA and extramural partners will begin soon. In addition, further experiments on the cellular and molecular events in restenosis are being conducted in animals as comparative testing of paclitaxel and radiation therapy for preventing restenosis gets underway.

As exciting new approaches like these are developed, important research also is underway to assess how medical practice and the public use new and even standard treatments. Unfortunately, prescription therapies on pharmacists' shelves today are not always being used effectively, as some studies on CVD demonstrate. Only an estimated 25 percent of Americans age 60 and older have their blood pressure under control, despite considerable evidence that high blood pressure can lead to heart attack, stroke, heart failure, and other serious health consequences.

In one study, a higher blood pressure level (defined as greater than 140/90mmHg), in people already being treated, was directly related to an increased risk of heart attack, leading the study's scientists to suggest that developing new strategies to improve blood pressure control might prevent an estimated 15 percent of heart attacks among older people with hypertension. An investigation

looking at use of warfarin, a drug used to inhibit blood clotting, showed it, too, was vastly under-prescribed for older people. The medication is known to dramatically reduce the risk of stroke in patients with the heart rhythm abnormality atrial fibrillation (AF). Yet, about 38 percent of those with AF and at least one other additional stroke risk factor, described by researchers as "ideal" candidates for warfarin, did not receive the drug when it would have been appropriate.

ENHANCING MUSCULOSKELETAL FUNCTION

It is a portrait that many of us have of aging — a stooped posture and frail appearance, slow gait, or more general problems with physical function, such as difficulty getting up from a chair. In recent years, dramatic reductions in the rate of disability have changed this picture for the better. Despite such progress, however, age-associated changes in bone and muscle and diseases common to advancing age still take a significant toll. Osteoporosis, osteoarthritis, and age-related loss of muscle mass make it difficult for older people to get around and, in many cases, to remain independent.

A number of elements make up the effort to combat what has been called "physical dysfunction." As in other aspects of biomedical research, scientists are looking beyond traditional study methods, trying to come up with better and more reliable ways to conduct research. Studies of bone and muscle can involve painful and invasive muscle biopsies, for example, and scientists are looking at better technology and more patient-friendly ways to measure, where possible, what happens to muscle with age. One approach involves use of new and sensitive imaging methods to look at fatty infiltration of skeletal muscle that occurs with age, a contributor to metabolic problems and muscle dysfunction. Scientists are now successfully testing magnetic resonance spectroscopy (MRS) and computerized tomography (CT) as a way to characterize fatty infiltration of skeletal muscle. The advance is welcome both for the comfort of study participants and for improving measurement in this area.

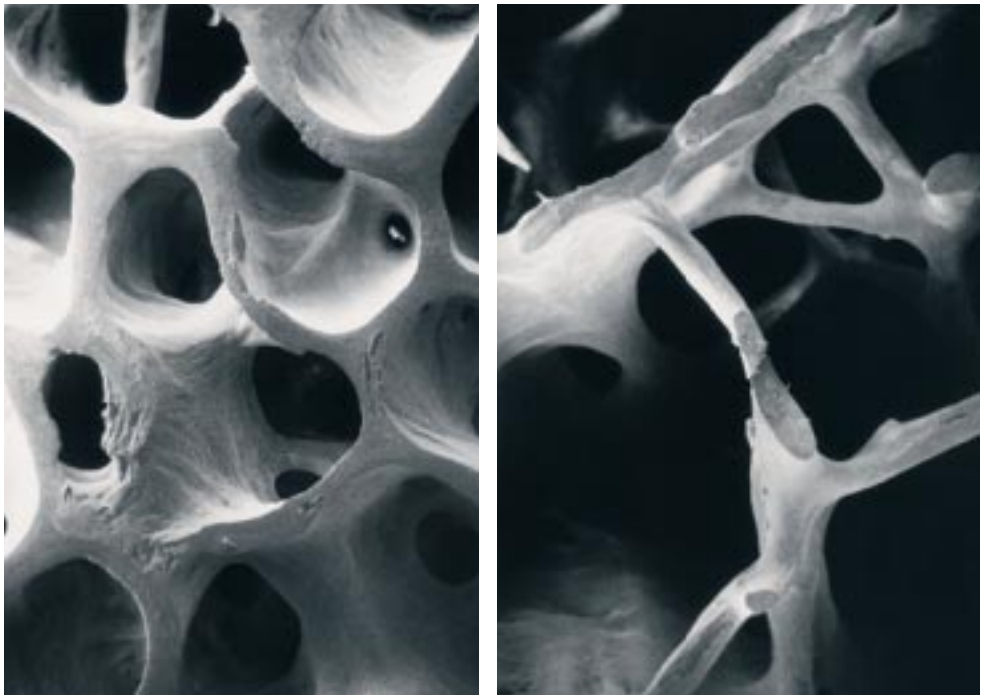
Studies in recent years have shown that changes in bone composition and quality, a loss of supporting and protective skeletal muscle, or a combination of the two can lead to falls, weakness, frailty, and ultimately fractures. A number of studies, many by researchers at NIA-supported Claude D. Pepper Older Americans Independence Centers, examine strategies, from exercise interventions to hormone therapies, for maintaining and improving physical function with age. For example, there has been some controversy about whether older people with osteoarthritis of the knee should increase or decrease their level of activity to keep frailty at bay. Research at one Pepper Center demonstrates that exercise can reduce risk for disability significantly. Among people 60 and older with

IT IS A PORTRAIT MANY OF US HAVE OF AGING — A STOOPED POSTURE AND FRAIL APPEARANCE, SLOW GAIT, OR DIFFICULTY IN GETTING UP FROM A CHAIR.

A NEW GENERATION OF DIABETES TREATMENTS IS UNDER INTENSIVE STUDY.

osteoarthritis, an 18-month strength training program reduced the risk of disability by 40 percent and an aerobic exercise program cut the risk by 47 percent.

New approaches may also be in order on hormones and osteoporosis. A study by investigators at another Pepper Center on estrogen replacement therapy (ERT) for osteoporosis has discovered that low-dose estrogen reduces bone breakdown in older women. Women age 65 and older took three different dosages of estrogen, and researchers measured changes in their bone over 6 months. Low-dose estrogen — at less than half of the dosage commonly used in ERT — surprisingly reduced bone breakdown as effectively as the highest dose, the researchers found. Importantly, side effects were significantly less frequent. The study suggests that low-dose estrogen could offer women the benefits of less bone breakdown while avoiding problematic side effects.



Normal bone (left); Osteoporotic bone (right).

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MANAGING DIABETES

Type 2 diabetes mellitus, the most common form of the disease, starts to develop in adults over age 40. It is caused by inability of beta cells in the pancreas to compensate for increasing insulin demands, resulting in raised blood sugar levels. A new generation of diabetes treatments, compounds that act on the pancreatic beta cells to secrete and produce more insulin and prevent the progressive rise in blood glucose, is under intensive study. Scientists at NIA's Laboratory of Clinical Investigation, with researchers in the private sector, have turned their attention to a substance called exendin-4, a compound derived from the saliva of the Gila monster lizard. It has many of the same properties of GLP-1, a peptide of the gut that has already been shown to stimulate beta cells to produce more insulin. The biologic activity of GLP-1 is short, however, and its effects quickly wear off. Tests in rats and mice show exendin-4 to be long-lived and more potent. Preliminary studies in small numbers of people with and without diabetes have demonstrated that exendin-4 can induce insulin secretion and normalize blood sugar. In the near future, an exendin-like drug might possibly become an effective treatment for type 2 diabetes.

Scientists are also looking at new ways to possibly intervene against diabetes before it

develops. One focus is insulin resistance, a metabolic condition thought to precede the development of type 2 disease in older adults. In insulin resistance, levels of insulin and of blood glucose are abnormally high, although not quite meeting the standards of diagnosis for diabetes. Obesity and sedentary lifestyle are the most serious risk factors for insulin resistance and researchers are now zeroing in on the possibility that changes in fat metabolism, particularly elevated levels of free fatty acids as the body breaks down fat, may interfere with normal glucose metabolism and contribute to insulin resistance. Studies of certain drugs and physical activity are promising in altering fat metabolism and interfering with the development of insulin resistance. These studies suggest that correcting age-related changes in fat metabolism may be important for proper treatment of older diabetics.

TREATING CANCER

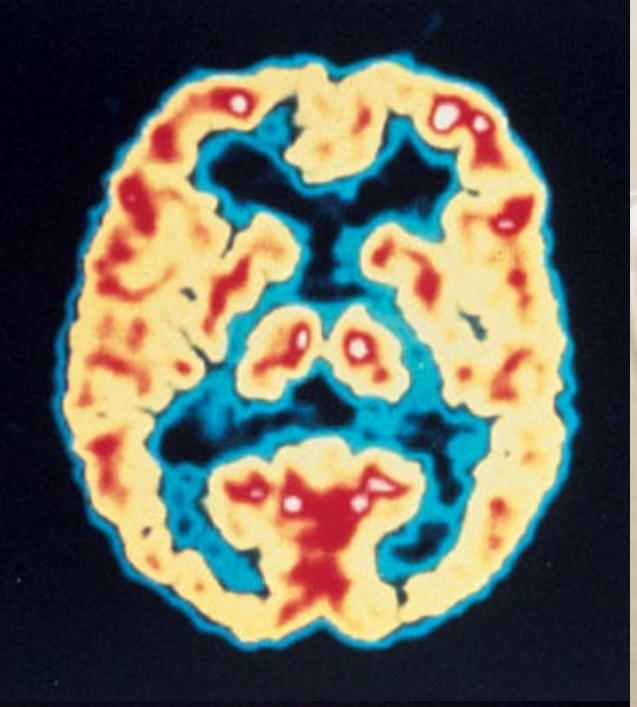
Cancer is the second leading cause of death in older people, yet some population-based data demonstrate a systematic bias against older patients resulting in their failure to receive potentially life-extending therapy. For example, in a recent study, half of people over age 65 with node-positive colon cancer were not treated with 5-fluorouracil-based adjuvant therapy despite the fact that such therapy reduces cancer mortality by more than one-third.

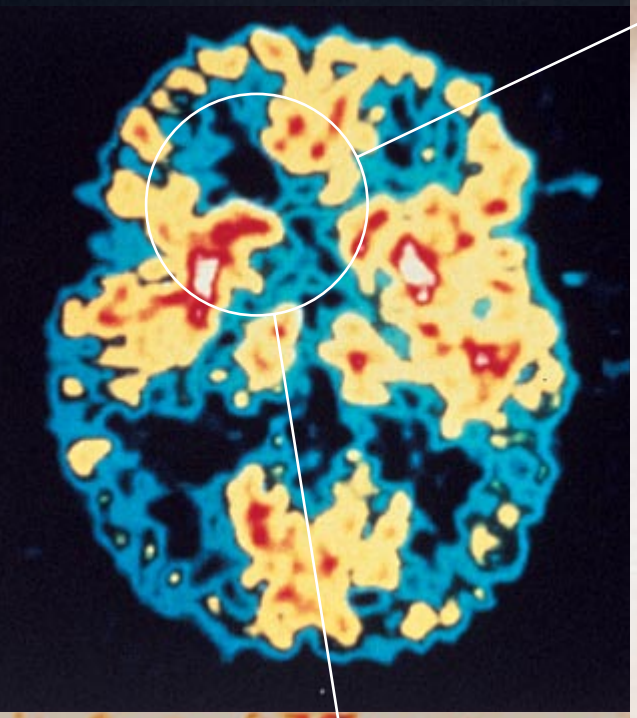
Older women with breast cancer may also find that their age has an impact on their cancer trajectory, prognosis, and treatment. NIA researchers, in conjunction with the NCI, recently concluded an analysis indicating that older women who had other health problems when they were first diagnosed with breast tumors received less aggressive cancer treatment and pretreatment assessments than women who were younger and healthier. NIA and NCI are collaborating on a variety of research initiatives to expand research on the major cancers common to seniors. Older people are entitled to receive the benefits of therapeutic advances and should actively seek advice from more than one physician in making critical decisions.

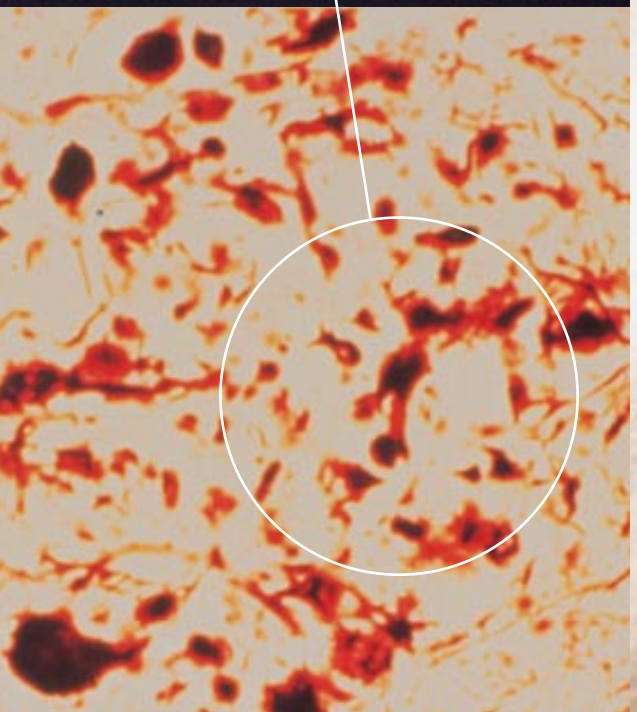
AN IMPORTANT MISSION OF NIA IS THE DEVELOPMENT OF A CORPS OF SCIENTISTS INTERESTED IN AND TRAINED TO STUDY AGING.

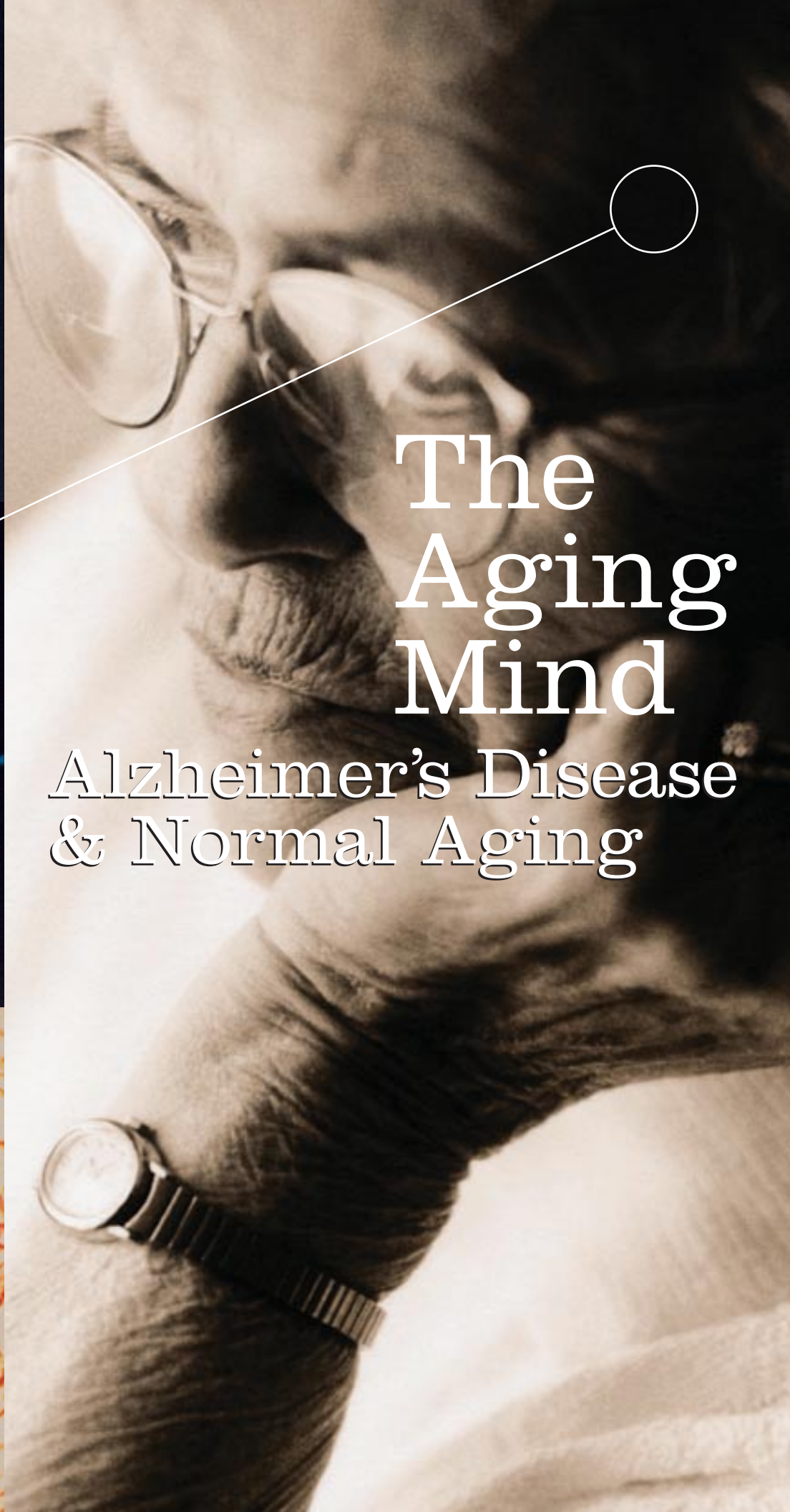
THE FUTURE OF CLINICALLY-FOCUSED RESEARCH

These disease and process-specific studies are not the only way that NIA addresses issues of aging and health. Research can only be as successful as the talent and dedication of scientists engaged in such studies. An important mission of the Institute is development of a corps of scientists interested in and specially trained to conduct studies of aging and age-related issues. NIA actively sponsors fellowship and training programs for junior and senior scientists at its laboratories in Baltimore, MD, and in research facilities at universities and other institutions across the U.S. One major effort was the establishment a decade ago and continued support for the Claude D. Pepper Older Americans Independence Centers.









The Aging Mind

Alzheimer's Disease & Normal Aging

ALZHEIMER'S DISEASE DEVELOPS AS A RESULT OF A COMPLEX CASCADE OF EVENTS.

The Aging Mind

Alzheimer's Disease & Normal Aging

Dr. Marcelle Morrison-Bogorad vividly remembers her first encounter with the human side of Alzheimer's disease (AD), the devastating deterioration of the brain that robs its victims of memory and, ultimately, identity. Dr. Morrison-Bogorad had trained in molecular biology, but soon found herself focusing on study of the development of the brain and, later, on brain aging and AD. Her work on AD brought her in contact with representatives from the local and national Alzheimer's Association, where Dr. Morrison-Bogorad advised the groups on technical issues and helped the organization in explaining scientific research to the families and friends of AD patients and to the public.

Leaving the shelter of the laboratory to meet her first AD patient was a shock, Dr. Morrison-Bogorad recalls. "I was thunderstruck. Here was this great, hulking man, and his wife had to talk to him and help him as if he were an infant. The blank look in his eyes was the most memorable, and disturbing." Her Scottish accent thickens and the look in her own eyes intensifies: "You only have to meet and talk with AD patients and their families to understand how much we need to stop it."

Today, Dr. Morrison-Bogorad is NIA Associate Director, Neuroscience and Neuropsychology of Aging Program, where she and her colleagues in the neurosciences program oversee hundreds of grants in support of universities and other institutions studying both the diseased and the normal aging mind. The program works in concert with neuroscience researchers at the NIA's in-house Intramural Research Program. In that program, led by Dr. Mark Mattson at the Laboratory of Neurosciences in Baltimore, MD, and Dr. John Hardy at the Laboratory of Neurogenetics in Bethesda, MD, scientists are tackling a number of innovative approaches to AD and neurodegenerative diseases.

In addition, NIA collaborates with other parts of the National Institutes of Health involved in neurological research, including the National Institute of Neurological Disorders and Stroke (NINDS), the National Institute of Mental Health (NIMH), and the National Institute of Nursing Research (NINR). These Federal activities provide a base for and stimulate research by the private sector as well, in which groups such as the Alzheimer's Association, and pharmaceutical, biotechnology, and other companies are also active in the search for effective treatments for AD.

There is an increasing urgency to these efforts. It is estimated that up to 4 million

people currently may have AD. And the prevalence of the disease — the number of people with AD at any one time — doubles every 5 years beyond age 65. It is expected that the number of people with AD will increase with the rapid growth in the older population. The cost to society of caring for AD patients is believed to be as much as $100 billion per year in direct and indirect costs. The human toll on AD patients and the informal network of family and friends in charge of their care is inestimable.

THE STUDY OF CAUSES AND RISK FACTORS IS BEGINNING TO DRAW A ROADMAP FOR HOW WE MIGHT PREVENT ALZHEIMER'S DISEASE OR AT LEAST DELAY ITS ONSET.

For some time, scientists have understood that AD develops as a result of a complex cascade of events taking place over a period of time inside the brain and influenced by both genetic and non-genetic factors. Today's research digs deeper into these events, to determine their sequence and pinpoint the various risk factors that may play a role. There is a new focus, too, on the study of normal changes in the brain and in cognitive function with age, which may help to further differentiate between the simple forgetfulness that we associate with aging and more serious diseases like AD. The pace and progress of research against AD have quickened in the past couple of years. "I believe we are gaining ground, but a lot more needs to be done," says Dr. Morrison-Bogorad.

Neuroscience research at the NIA is organized into broad and overlapping areas. The focus on AD looks at causes and risk factors, diagnosis, treatment, and caregiving. Expanded efforts to understand healthy brain aging also could provide insights for maintaining cognitive function and protecting against dementia.

ALZHEIMER'S DISEASE CAUSES AND RISK FACTORS

New understanding from the study of causes and risk factors is beginning to draw the roadmap for how we might prevent AD or at least delay its onset. Basic work is expanding our knowledge of AD genetics. There have been major breakthroughs in identifying genetic mutations responsible for early onset AD and genetic influences that may be risk factors for late onset AD. Mutations of genes on three separate chromosomes that can cause early onset AD have been discovered and scientists are on the trail of additional genetic risk factors for late onset forms of the disease beyond the known risk factor gene APOE ε4. New technologies will allow scientists to home in on more genes more quickly to learn even more about the molecular processes underlying the disease. This research may lead one day to treatment strategies tailored to an individual's unique genetic profile.

Amyloid plaques and neurofibrillary tangles are the hallmarks of the disease in the brains of AD patients. New insights into the etiology of the disease explain their formation and role. The knowledge from early studies that a protein, the amyloid precursor protein, is mutated in some early onset AD has led to a research focus on amyloid. Recently, scientists zeroed in on the identity of enzymes called secretases, which it is now believed "clip" the amyloid precursor protein to produce a beta amyloid peptide that forms the plaques. Supported by both the public and private sector, this research is leading to development of a new generation of secretase-inhibiting drugs, some of which are now being tested.

An intensified area of study looks at tau, a protein that forms the tangles involved in AD. A new "transgenic" mouse with human tau mutations that cause another form of dementia may help scientists to understand better why tangles form and the role they play in the death of neurons (brain cells) and the development of dementia. One group of researchers has taken the mouse model a step further, engineering one with both plaques and tangles in brain regions that are characteristic of human AD, a breakthrough likely to yield important clues about the relationship between amyloid and tau.

Several factors are suspected to put us at risk of AD or protect against it. Aging is the major risk factor, followed by being a blood relative of someone with AD. Head injury is also linked with increased risk. What else in our health and environment, including factors that we can possibly control, can affect the development and course of AD? Under current study are the role of diet, education, and exercise and physical activity, among a variety of potential influences. Studies in groups of people and in animals, for example, have suggested a few ways in which plaque development might be influenced.

One study in mice looked at the relationship between cholesterol and levels in the brain of the beta amyloid peptide, known to predispose people to the formation of amyloid plaques. Mice were fed both high and low

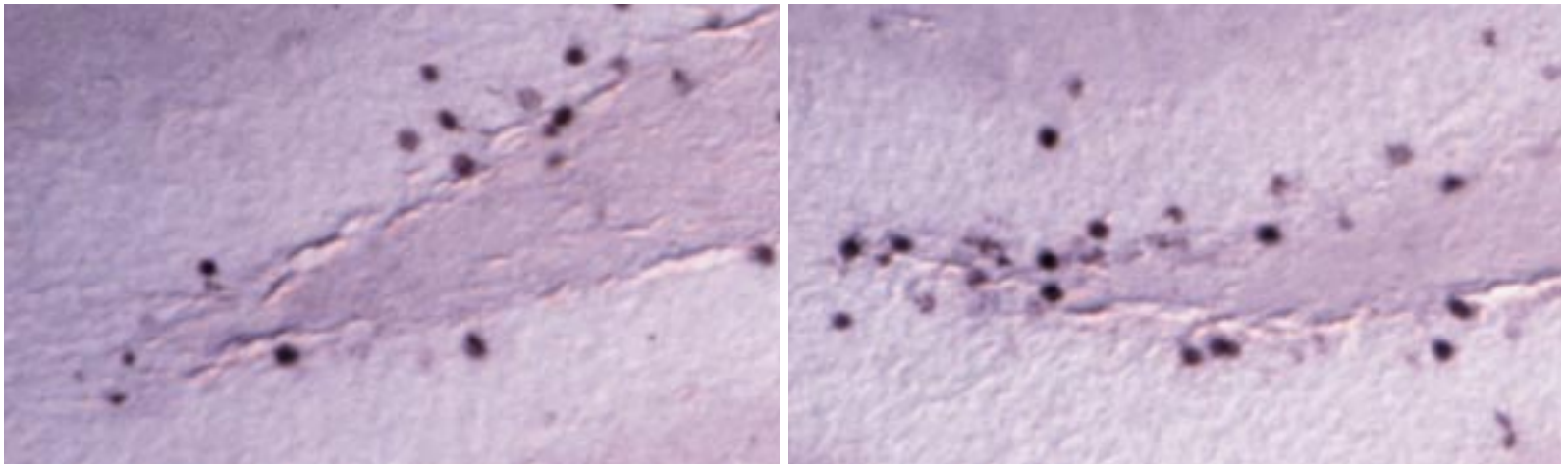
MANY OF US HAVE WONDERED WHETHER SIGNS OF FORGETFULNESS ARE NORMAL OR THE START OF A MORE SERIOUS MEMORY OR COGNITIVE PROBLEM.

RESEARCHERS BELIEVE THAT NEURAL STEM CELLS PROVIDE A CELLULAR "RESERVOIR" THAT CAN BE TAPPED TO REPLACE LOST OR DAMAGED NEURONS.

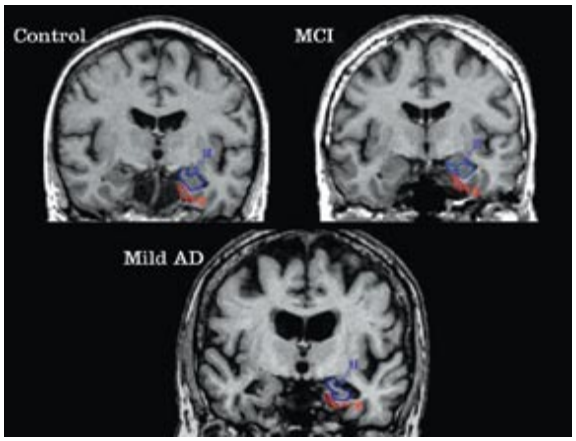
cholesterol diets for 7 weeks. At the end of the study, the mice on high cholesterol diets had more cholesterol in their blood and brains, and beta amyloid peptide levels and plaques were also increased. This study is the first demonstration in a transgenic mouse that high blood cholesterol levels markedly increased amyloid "burden" in the brain. In people, epidemiological research on the possible cholesterol-AD connection has shown that those taking cholesterol-lowering drugs called statins appear to have a lower risk of AD than those untreated. These studies are sparking increased interest in the role that blood lipids such as cholesterol might play in AD and are turning researchers' attention to the possibility that cholesterol-lowering drugs could reduce the risk for dementia.

Experiments by Dr. Mattson and scientists at NIA's Laboratory of Neurosciences provide the first evidence in laboratory animals that calorie restriction can increase the resistance of neurons to stresses associated with disease and aging. How calorie restriction produces these effects is yet unknown, but recent findings suggest that a low calorie diet stimulates the production of neurotrophic factors, proteins that promote the survival and growth of neurons. "Eventually, we may find a way to mimic the benefits of caloric restriction to reduce neuronal damage and have an effect on neurodegenerative disorders in humans," says Dr. Mattson.

The neurosciences laboratory also is focusing on neural stem cells, a type of cell that can divide repeatedly and then form new neurons. Such stem cells are present in the brains of adult rodents and humans, and it is believed that they provide a cellular "reservoir," as researchers describe it, that can be tapped to replace lost or damaged neurons. An exciting and rapidly advancing area of research, studies of neural stem cells suggest that they can be mobilized by calorie restriction. NIA-funded researchers have also found in mice that "intellectual activity" may stimulate stem cells to produce more neurons, in experiments comparing mice in a normal laboratory environment with those in an enriched environment of toys and other objects. These studies, notes Dr. Mattson, suggest that the production of new neurons might be modified by diet or activities that stimulate the brain intellectually.



An enriched environment stimulates stem cells in the brain to produce more neurons. (Control sample, left, and enriched sample, right.)



DIAGNOSING ALZHEIMER'S DISEASE

At one time or another, many of us have wondered—for ourselves or a loved one—whether signs of forgetfulness are normal or the start of a more serious memory or cognitive problem. One way scientists are tackling this question is by studying the difference between normal cognitive aging and early signs of AD. This particularly active area of research involves the imaging of brain structure and function and testing for a variety of cognitive abilities in order to identify as early as possible people at highest risk for AD. These diagnostic tools could be used to help clinicians and patients evaluate symptoms, and they will be useful for determining who should participate in clinical trials. Down the road, as therapies are developed and we are better able to intervene early in the disease process, early diagnosis will be critical for targeting specific treatments to people most at risk.

Scientists are especially interested in trying to identify people who might have Mild Cognitive Impairment (MCI). In MCI, people have demonstrable memory impairment but do not meet the established criteria for a diagnosis of AD. Eighty percent of people diagnosed with MCI in one study developed AD within 8 years. Imaging studies of people with MCI found that the smaller the hippocampus (a particular brain region associated with learning and memory) at the beginning of the study and the more rapidly the hippocampus shrinks with age, the more likely people were to develop AD within a few years when compared with people of similar age and health status.

A Framework for Finding Answers

To expand and expedite the search for causes and for treatments of AD, the NIA maintains and supports a nationwide infrastructure for research and assistance. This includes:

Alzheimer's Disease Centers (ADCs). Located at major medical institutions around the country, the 29 ADCs clinically evaluate and conduct research of AD patients and their families. Specifically, the Centers systematically collect and analyze longitudinal data on people with and without dementia; work to translate research advances into clinical practice; educate and train professionals in research, evaluation, and treatment of AD; and participate in clinical trials. Satellite centers strengthen the network, many recruiting minority participants to the Centers program.

The National Alzheimer's Coordinating Center (NACC). The center was established to collect and begin to standardize data collection from all the ADCs. The "strength in numbers" provided by this endeavor will enable researchers to conduct studies that would not be possible with the smaller number of participants in individual centers. The data will allow scientists to characterize earlier, preclinical stages of the disease and rarer forms of AD as well as possible genetic and ethnic differences. Currently, the NACC holds data from approximately 40,000 research participants evaluated at the ADCs since 1984.

Alzheimer's Disease Cooperative Study (ADCS). This consortium of some 31 academic medical centers, including most of the ADCs, conducts cooperative clinical trials on drugs to manage and treat the cognitive and behavioral symptoms of AD. It is designed to help speed up the movement of drug testing from epidemiological and laboratory research to the clinic, examining both currently available compounds and newly designed drugs for AD.

Drug Discovery Initiatives. NIA employs a number of ways to encourage the development and testing of new compounds to manage or prevent AD. The Institute funds small as well as regular research grants, small business innovation research grants, small business technology transfer grants, and contracts in this effort.

National Cell Repository. This is a growing repository of blood samples collected from AD patients and their families, an effort that facilitates the study of genetic defects associated with the disease. In addition, all of the ADCs maintain their own brain banks and banks of biological samples and have developed an extensive network of tissue sharing with other investigators.

Alzheimer's Disease Education and Referral Center (ADEAR). This information center is a central source for information on all aspects of AD. Information on how to contact ADEAR is at the end of this booklet.

New studies also suggest that it may be important to try to identify people at risk of AD, even before MCI develops. This work indicates that older people with MCI already have dramatic decreases in the number of neurons and a reduction in the volume of part of the brain's entorhinal cortex, which plays a crucial role in memory processing and which is one of the areas first affected in AD. These brain changes were associated with very early cognitive changes and suggest that damage to the brain in AD may start to occur long before the disease is diagnosed.

TREATING ALZHEIMER'S DISEASE

A decade ago, just a handful of medications for AD were being tested. Today, human clinical trials involve dozens of compounds. Under scrutiny are such well-known drugs as nonsteroidal anti-inflammatory drugs (NSAIDS) for their possible effectiveness against cognitive decline and AD and wholly new molecules designed to interrupt underlying mechanisms of the disease. These studies target three main treatment goals: prevent AD altogether or slow its development; maintain cognitive function in the short-term; and manage the difficult behavioral problems, such as agitation, aggression, wandering, and sleep disorders, associated with the disease.

In 2001, the NIA supported some 21 pilot and full-scale clinical trials for AD. Some of these studies are prevention trials to see if a particular treatment slows or prevents the onset of cognitive decline or diagnosed AD.

A DECADE AGO, JUST A HANDFUL OF MEDICATIONS FOR AD WERE BEING TESTED. TODAY, HUMAN CLINICAL TRIALS INVOLVE DOZENS OF COMPOUNDS.

Currently available compounds being tested include NSAIDs and aspirin, antioxidants such as vitamin E, combined folate/B6/B12 supplementation, and ginkgo biloba, which is being tested in a trial supported mainly by the NIH's National Center for Complementary and Alternative Medicine. In addition, estrogen replacement therapy is being evaluated to see if it might prevent AD in women with a family history of the disease.

As a result of greater understanding of the genetic, molecular, and cellular factors involved in AD, the design and testing of new therapeutic approaches is gaining momentum as well. Secretase-inhibiting drugs are a focus in the private sector and both public and privately funded researchers have stepped up efforts to further study and test a new vaccine against AD, which may protect against the formation of amyloid plaques altogether. The NIA has issued a request for new research applications to conduct further vaccine-related basic research. These studies, in animal models, should help to further understand the mechanisms and long-term effects of vaccines against AD. One pharmaceutical company is in the very early stages of testing a vaccine in humans.

CARING FOR ALZHEIMER'S DISEASE PATIENTS AND FAMILIES

Beyond the patient, AD takes a considerable toll on families, caregivers, and friends. The memory loss and altered emotions and behaviors associated with the disease are an almost impossible burden, posing an enormous physical and emotional challenge for caregivers. One recent survey indicates that caring for someone with dementia, compared with attending to someone with other types of illnesses, involves significantly more time spent on caregiving tasks, greater employment complications, caregiver strain, mental and physical health problems (including lowered resistance to disease) and family conflict, as well as less time for leisure and other family members.

Research on caregiving and long-term care examines ways to alleviate or prevent some of these problems. The effectiveness of support groups, behavioral skills training programs, family-based interventions, computer-based information and communications services is now being tested. Data are now being reviewed from a number of sites in the NIA- and NINR-supported REACH (Resources to Enhance Family Caregiver Health) initiative, which should provide important clues about what works—and what doesn't—to support families of patients with AD. Studies so far suggest that information and problem solving needs of caregivers change with time as the disease progresses and issues change. "The study of caregiving, with its mix of physical, emotional, and social and cultural factors, is an especially challenging one for research," notes Dr. Morrison-Bogorad. The Institute works closely with the Alzheimer's Association and other groups to share research findings on caregiving and other aspects of AD and aging.

THE EMOTIONS AND BEHAVIORS ASSOCIATED WITH ALZHEIMER'S DISEASE POSE AN ENORMOUS PHYSICAL AND EMOTIONAL CHALLENGE FOR CAREGIVERS.

STUDIES OF LEARNING REVEAL THAT OLDER ANIMALS AND PEOPLE CAN LEARN NEW INFORMATION WELL, BUT ACQUIRE IT MORE SLOWLY THAN YOUNGER ADULTS.

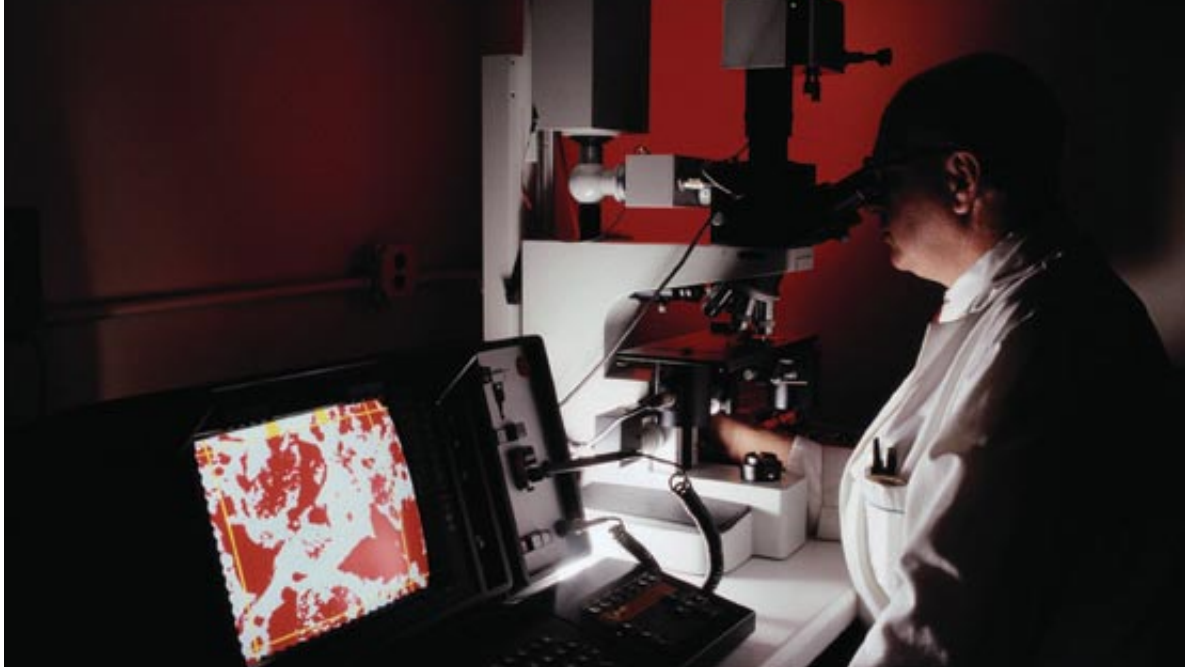
NORMAL AGING OF THE BRAIN

Scientists are also intensifying their focus on normal aging of the brain. Research to date indicates that overall structural integrity, in many regions, appears largely to be preserved as we grow older. Contrary to what was once thought, there is no general neuron loss with age and there are parts of the brain, such as the hippocampus, where new neurons are formed well into old age. But there is increasing evidence that cellular and molecular changes take place in the brain over time. And many changes in brain-related functions have been measured in older adults, such as non-dementia memory loss and cognitive declines; "tip-of-the-tongue" problems; impairments in vision, hearing, and taste; and changes in sleep rhythms and sleep quality.

The risk for cognitive impairment, for example, is known to increase with age. Complex cognitive behaviors of attention, language, learning, and memory become vulnerable to insults. This can result in declines in performance of everyday tasks such as driving or managing finances, causing frustration and concern among older people and often leading to isolation from loved ones and society. At their worst, problems at first viewed as normal changes with age can become severe enough to be classified as MCI and, ultimately, as AD.

To understand these changes, scientists are pursuing several avenues of study. Studies of learning, for example, reveal that older animals and people can learn new information well, but acquire it more slowly than younger adults. In some studies, old rabbits need many more tries to learn a new response than their younger counterparts. Analysis of brain cells from these animals shows that while the nerve cells from the older animals do still function, the cells actually have to rest longer between episodes of communication with one another. Further study indicates that this change is due to an impaired ability of the older nerve cells to control how much calcium enters the cell. Age-related problems in learning improve when the excess entry of calcium into the cell is blocked.

Healthy older people can have attention deficits as well, particularly when they have to divide their attention among two or more things. In one study of visual attention and reaction time, it took older adults more time to focus on a particular item, such as a specific letter, than younger people. The older adults were less able to ignore competing but irrelevant information, such as other letters in their field of view.



The use of neuroimaging technologies is an exciting development in research on brain changes and function. It allows scientists to look deep inside the brain during performance of cognitive tasks. In several studies, older adults show activation of more brain regions in the frontal cortex of the brain than younger adults during performance of a short-term memory task. The different pattern of brain activity between older and younger adults doing the same task may have a number of explanations, researchers say. Perhaps the older brain needs to "recruit" more areas in order to successfully accomplish a cognitive task. It also may be that the older brain engages in different strategies to do a task, strategies that stem from years of experience. Scientists believe that use of imaging in these types of psychological and neurological research will reveal much more about the direct relationship between brain changes and our ability to perform cognitive tasks. Such research will lead to development of effective ways to help maintain brain function.

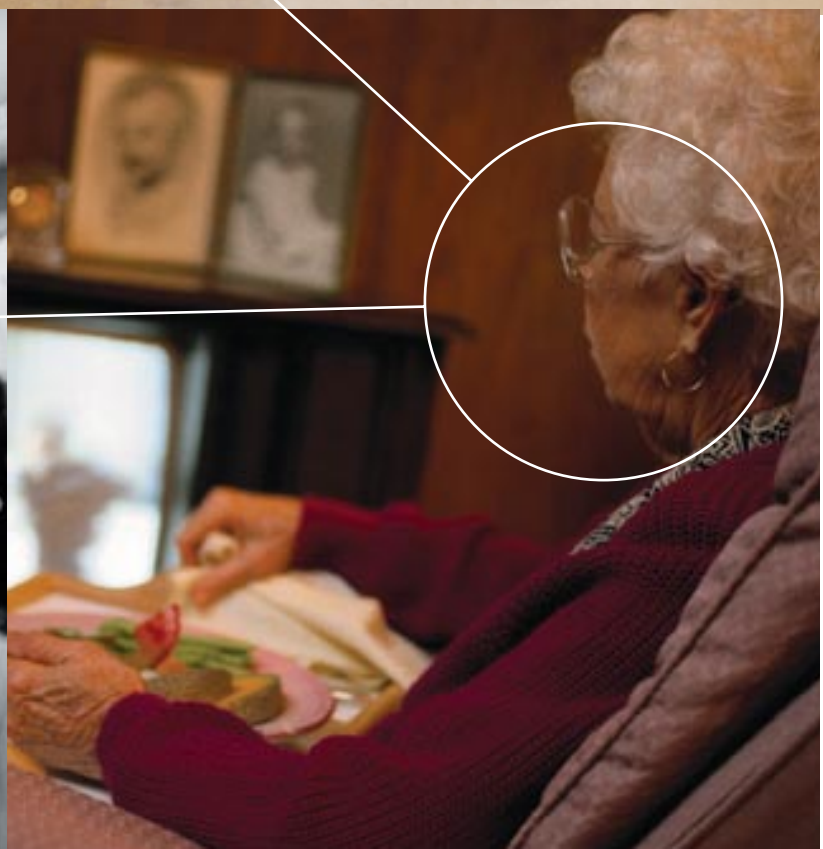
Results up to now from such human and animal research have been promising, but much more needs to be discovered. Toward that end, the Institute is part of a new "Healthy Brain Project" initiative, bringing together NIA, NINDS, and NIMH to learn more about the cognitive and emotional health of older adults. Researchers hope that the effort can accelerate the pace of scientific advances in the study of cognition and emotion and their effects on well-being as we age.

THE OVERALL STRUCTURAL INTEGRITY OF THE BRAIN APPEARS TO BE PRESERVED, BUT THERE IS EVIDENCE THAT CELLULAR AND MOLECULAR CHANGES TAKE PLACE OVER TIME.

INFORMATION ON ALZHEIMER'S DISEASE AND BRAIN AGING

For the latest information on AD, the NIA operates the Alzheimer's Disease Education & Referral (ADEAR) Center, a service devoted to providing information on memory and dementia, specifically AD. The Center, mandated by Congress, serves health professionals, patients and their families, the media, and the public. It provides general publications on AD and annually prepares a *Progress Report on Alzheimer's Disease*, describing research efforts on dementia and AD supported and conducted across the National Institutes of Health. ADEAR also offers referrals to NIA-funded Alzheimer's Disease Centers across the U.S. that specialize in research and patient diagnosis. It can conduct custom searches from the Combined Health Information Database (CHID) and provide training and resource materials for physicians, nurses, and other health care workers. Contact information for the ADEAR Center and the NIA's general aging Information Center appears at the end of this booklet.

Behavioral & Social Aspects of Aging



Behavioral & Social Aspects of Aging

Personal behavior and lifestyle choices — whether or not we smoke, or exercise, or take prescribed medicines, even our individual personalities — make a major difference in health and well-being in later life. Society's decisions about such things as access to health care or pension and retirement policy, also significantly impact how we age. As the power of these influences, along with the effects of education and wealth, are more evident, behavioral and social research has become an energized area of study. From large national surveys of population trends to research delving into how individuals approach their own aging, behavioral and social research provides intriguing and useful insights into ourselves and the world around us. Armed with such knowledge, scientists seek to inform social policy and develop interventions for improved health.

The interplay among health, behavior, and socioeconomic factors is a particular focus of NIA's nationwide Health and Retirement Study (HRS). In the mid-1980s, Dr. Richard Suzman, now NIA Associate Director, Behavioral and Social Research Program, joined by a small group of other leading experts in health and economics, began to realize that research on retirement and on health essentially treated these two aspects of aging as if they had nothing to do with each other. Dr. Suzman and his colleagues thought of retirement as a process well beyond simply collecting a pension or Social Security. "It was very clear to us that more needed to be known about the dynamics preceding and during retirement, especially the interrelationships of health, disability, economics, work, and family," he says.

After much discussion and careful design, in 1992, the HRS, one of the largest and most innovative surveys ever conducted in the U.S. on health and retirement, began interviewing participants. Today, the study is conducted by the University of Michigan's Institute for Social Research, which every 2 years surveys about 20,000 Americans age 51 and older about work, health status, disability, pensions and retirement, family relationships, community activities, and other selected aspects of aging.

Scientists are now mining the rich fields of data provided by the HRS. The study has helped define the relationship between health and wealth, suggesting that, throughout life, the dynamic appears to cut both ways — wealth influences health, but poor health also affects the accumulation or loss of wealth in later years. Surprisingly, the HRS findings indicate that a significant percentage of older people support their adult children financially and in other ways, such as caring for grandchildren, challenging the common view of a dependent elderly population. The HRS also

hints that employers and pension planners might want to rethink the transition into retirement: about half of people nearing retirement say they would prefer to phase out of the workplace, rather than to quit "cold turkey," as is often the case today.

Over the next few years, the HRS is expected to address a number of significant questions. How well, for instance, are the so-called "baby boomers" prepared for retirement? How will changes in Social Security, Medicare, and Medicaid affect older Americans and their families? What impact will the high rate of divorce in recent years have on pensions and, equally important, on caregiving in later life? "I believe the HRS can play a central role in telling the story of the aging baby boom," says Dr. Suzman. He points out that some other developed countries are now using the HRS as a model for studies of their aging populations as well.

The NIA plays a leading role in funding a variety of major demographic studies and in assuring that national surveys related to aging, health, and retirement are technically sound and useful to the public and policymakers. In 1994, NIA established its Centers on the Demography of Aging at research institutions around the country to improve the quality and relevance of demographic research on health, economics, and population aging. In 2001, NIA supported 11 such centers, each characterized by its own focus or specialization.

BEHAVIORAL AND SOCIAL RESEARCH PROVIDES INTRIGUING AND USEFUL INSIGHTS INTO OURSELVES AND THE WORLD AROUND US.

In the mid-1980's, NIA helped found the Federal Interagency Forum on Aging-Related Statistics. The Forum works closely with the Bureau of the Census, the National Center for Health Statistics, and other Federal statistical agencies on the quality, collection, and confidentiality of data on older people from government-supported studies.

In July 2000, the Forum published its first status report on aging in America, *Older Americans 2000: Key Indicators of Well-Being.* Based on a review of more than a dozen national data sets, it found that while there is good news about gains in health and wealth among older people, a large proportion of the older population, including many racial and ethnic minorities, still face disability, chronic health problems, and economic stress.

NIA's support of behavioral, psychological, and social research casts a very wide net, as it examines everything from personality to populations. This research looks at the spectrum of possible influences on longevity, health, and behavior, including potential biological and genetic factors that may play a role. A few areas of growing interest are highlighted here — the role that personality and attitudes might play in late-life health, including cognition, and how public health might be improved with greater understanding of individual health behaviors and of the changing patterns of health and mortality.

PERSONALITY AND SOCIAL/ BEHAVIORAL INFLUENCES ON HEALTH

On the most individual level, can personality and outlook affect your risk of disease or death? Studies of personality suggest that it can. Led by Dr. Paul T. Costa, Jr., chief of the NIA's Laboratory of Personality and Cognition, NIA's researchers have developed a model to provide a way to characterize personality, examine its effects, and measure possible personality-specific interventions against disease and disability. This Five-Factor Model is a comprehensive characterization of five key dimensions — neuroticism, extraversion, openness, agreeableness, and conscientiousness. For example, new data from the Five-Factor Model questionnaire identify several dimensions of personality associated with success or failure to achieve adequate compliance with a drug regimen. In a specific case, studies are now underway to measure personality traits that are linked to complying with anti-retroviral therapies for HIV/AIDS. "By identifying individuals whose questionnaire responses show they are prone to experience stress and have poor self-discipline, we can target these patients for special interventions," says Dr. Costa.

It is also important to obtain information on personality from older people unable to respond to questionnaires, such as those with dementia. New tools developed by scientists at the NIA's laboratory open a window for scientists to assess the previously unmeasured impact of dementing disorders on personality. This "observer-rating" form of the Five-Factor Model questionnaire has been used in a number of studies in the U.S. and Europe to look at patients with Alzheimer's disease (AD), Parkinson's disease, and traumatic brain injury. Information from caregivers and family members shows that patients with these diseases undergo significant changes in personality. In AD, for example, personality changes reflect diminished capacity for organization, punctuality, dependability, goal-setting, and planning. Ongoing studies will attempt to determine the ordering of these personality changes, whether they occur before the disease becomes evident

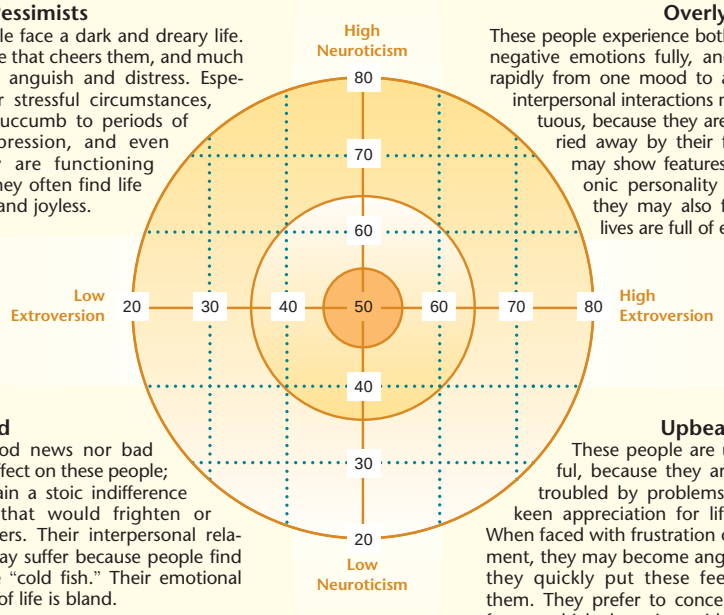
Personality styles are defined by combinations of factors. Two of 10 combinations are illustrated here.

Style of Well-Being

Vertical Axis: Neuroticism (N) / Horizontal Axis: Extraversion (E)

N+E-
Gloomy Pessimists
These people face a dark and dreary life. There is little that cheers them, and much that causes anguish and distress. Especially under stressful circumstances, they may succumb to periods of clinical depression, and even when they are functioning normally, they often find life to be hard and joyless.

N+E+
Overly Emotional
These people experience both positive and negative emotions fully, and may swing rapidly from one mood to another. Their interpersonal interactions may be tumultuous, because they are so easily carried away by their feelings. They may show features of the histrionic personality disorder, but they may also feel that their lives are full of excitement.



N-E-
Low-keyed
Neither good news nor bad has much effect on these people; they maintain a stoic indifference to events that would frighten or delight others. Their interpersonal relationships may suffer because people find them to be "cold fish." Their emotional experience of life is bland.

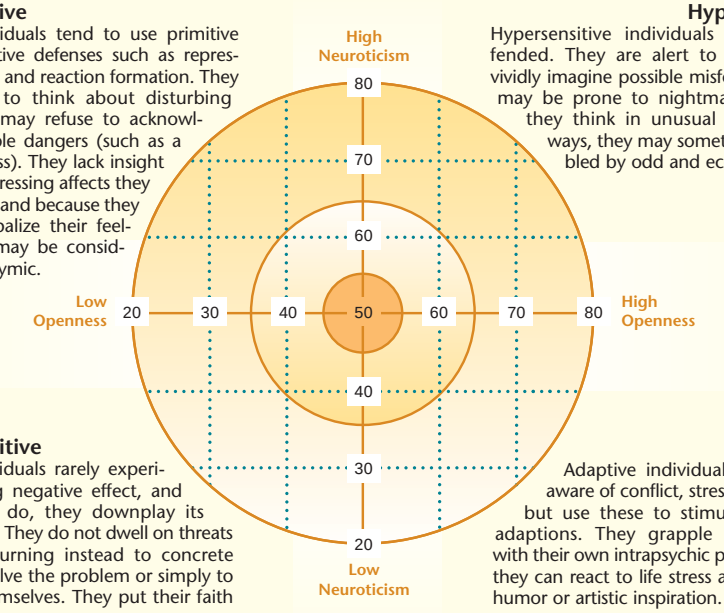
N-E+
Upbeat Optimists
These people are usually cheerful, because they are not unduly troubled by problems, and have a keen appreciation for life's pleasures. When faced with frustration or disappointment, they may become angry or sad, but they quickly put these feelings behind them. They prefer to concentrate on the future, which they view with eager anticipation. They enjoy life.

Style of Defense

Vertical Axis: Neuroticism (N) / Horizontal Axis: Openness (O)

N+O-
Maladaptive
These individuals tend to use primitive and ineffective defenses such as repression, denial, and reaction formation. They prefer not to think about disturbing ideas, and may refuse to acknowledge possible dangers (such as a serious illness). They lack insight into the distressing affects they experience, and because they cannot verbalize their feelings, they may be considered alexithymic.

N+O+
Hypersensitive
Hypersensitive individuals seem undefended. They are alert to danger, and vividly imagine possible misfortunes. They may be prone to nightmares. Because they think in unusual and creative ways, they may sometimes be troubled by odd and eccentric ideas.



N-O-
Hyposensitive
These individuals rarely experience strong negative effect, and when they do, they downplay its importance. They do not dwell on threats or losses, turning instead to concrete action to solve the problem or simply to distract themselves. They put their faith in higher powers.

N-O+
Adaptive
Adaptive individuals are keenly aware of conflict, stress, and threat, but use these to stimulate creative adaptions. They grapple intellectually with their own intrapsychic problems, and they can react to life stress as a source of humor or artistic inspiration.

or whether they follow memory changes. Scientists are also hoping to determine if personality changes might be an early marker for the start of special interventions or treatment for dementia.

It may be that how we look at life can affect how we age. A study of 1,002 disabled women age 65 and older participating in the NIA-sponsored Women's Health and Aging Study found that "emotional vitality," that is, a sense of personal mastery, being happy, and having low anxiety and depression, is linked with reduced risk of further disability and even death. Recent findings from the Nun Study, a longitudinal survey of older Catholic Sisters, found a strong relationship between positive emotions expressed in early life writings and reduced risk of death in their 80s and 90s. In the study, handwritten biographies written by 180 nuns in their 20s were evaluated for positive emotional content and then were related to survival. This growing body of research suggests that we might press beyond looking at depression and other aspects of emotional dysfunction to study the role that positive emotions may play in health and longevity.

Researchers are also looking at how social and behavioral factors might affect cognition. According to a number of studies, cognitive ability — the process of thinking, learning, and remembering — can decline with age. This is of concern because cognitive skills are critically important in allowing older people to maintain their vitality and independence.

Social and behavioral influences on cognition may be considerable, according to current research. In one study, older adults were exposed, without being directly aware of it, to both positive and negative stereotypes about aging. Researchers created scenarios using words such as "wise" or "senile," for example, and then tested participants immediately on a variety of measures. On both cognitive tests and physiological measurements, older adults exposed to negative stereotypes about aging performed poorly when compared with those exposed to positive stereotypes. Researchers are now looking at ways to further test the

COGNITIVE SKILLS ARE CRITICALLY IMPORTANT IN ALLOWING OLDER PEOPLE TO MAINTAIN THEIR VITALITY AND INDEPENDENCE.

From Lab Bench to Bench Press: NIA Launches an Exercise Campaign

"From bench to bedside." It's an expression that health scientists and educators use in talking about how to take what is discovered at the laboratory workbench and make it a part of everyday medical practice.

As a practical matter, research should make its way into the public health consciousness, and NIA scientists and public information and health education experts constantly look for opportunities to communicate scientific results in the most effective way to the world outside the Institute's corridors. "Improving public health is really the bottom line for research," says Jane Shure, director of the NIA's Office of Communications and Public Liaison. "Sharing what we have learned, with clinicians and with the public, is an important part of that effort."

The Institute's national education campaign on exercise, notes Ms. Shure, is a model case in point. In 1998, the NIA, with astronaut and Senator John Glenn, and other Federal agency partners, launched a national education campaign for keeping fit after 50. The centerpiece of the campaign was publication of the important new book, *Exercise: A Guide from the National Institute on Aging.* By 2000, the enormously popular and award-winning publication had been made into a video version featuring exercise expert Margaret Richard. The print Guide is distributed free in single copies and the video is offered at cost. Some 370,000 booklets have been sent out and the video is quickly catching up. In 2001, the NIA published a Spanish language version of the exercise Guide. Other organizations have translated it into Japanese and French.

Why exercise? In 1996, when the idea of the project was raised, two key developments had taken place. First, research on exercise and its benefits for aging populations had reached a critical mass. Scientists were convinced that exercise could make a difference, and they had data on what specific exercises would work best. Second, NIA's public information staff noticed increased interest in healthy aging from the media and the general public, with a distinct focus on exercise. But in telling the press and the public about the benefits of exercise, it was difficult to follow up on the next logical questions: What type of exercises should people 50 and older do? How should they get started?

So, in September 1996, the NIA gathered an important panel of outside experts and its own scientific

Exercise Campaign

Continued from previous page

staff to answer these questions. It was agreed that the time was right to proceed with developing an exercise program that would fill the need for this information. The Guide was completed and printed in 1998, after a major scientific literature analysis, extensive writing and editing, and reviews and revisions incorporating the comments of more than 40 reviewers representing a broad expertise in health, aging, and exercise.

The NIA works intensively to get the exercise book into the hands and living rooms of middle-age and older people. Through public service announcements, participation in meetings of health and fitness educators and instructors, liaison with the medical community, and other marketing efforts, the Institute continues to shine the spotlight on exercise as one of the most effective interventions known for healthy aging.

The Guide and video, as well as NIA's general publications on aging, are distributed by the NIA Information Center. Contact information for the Information Center is located at the end of this booklet.

BECAUSE OF THEIR PROVEN BENEFITS ON HEALTH, WELL-BEING, AND LONGEVITY, PHYSICAL ACTIVITY AND EXERCISE ARE A MAJOR FOCUS OF STUDY.

study's findings that link negative age stereotypes to measureable health risk. They also suggest that the reverse may be true — positive self-images of aging might be employed to improve health, including cognitive performance. Maintaining close social relationships as we age may also relate to cognition. Studies are beginning to indicate that these relationships may help protect against declines in cognitive and physical function as well as positively affect longevity.

As scientists continue to examine what may threaten cognitive function in later life, NIA supports testing of potential of interventions to maintain it. The ACTIVE (Advanced Cognitive Training for Independent and Vital Elderly) initiative is an ongoing multi-site study in which more than 2,800 older adults receive training in skills related to memory, reasoning, and speed-of-processing. Participants will be tested over time to see if the training helps to maintain function or postpone cognitive decline.

PERSONAL BEHAVIORS AND POPULATION TRENDS IN HEALTH

Behavioral medicine deals with how people develop and maintain behaviors affecting health and illness. It examines the choices we make, almost daily, in lifestyle practices, managing ourselves medically, and, when we have to, coping with chronic disease or disability.

Because of their proven positive benefits on health, well-being, and longevity, physical activity and exercise are a major focus of study. An alarming 75 percent of older Americans do not engage in at least 30 minutes of physical activity a day, as national health guidelines suggest, and public health officials and advocates are in search of ways to turn that sedentary trend around. A key question for research: Once a couch potato always a couch potato? The answer is no, according to new studies in this area. Health behaviors can change at any age.

A KEY QUESTION FOR RESEARCH: ONCE A COUCH POTATO ALWAYS A COUCH POTATO? THE ANSWER IS NO, ACCORDING TO NEW STUDIES ABOUT PHYSICAL ACTIVITY.

In one test, researchers used a behaviorally based approach at an existing community program. Participants explored their reasons for not exercising and then drew up personal plans for increasing physical activity. Personal attention and telephone calls from staff, plus an informational meeting, were found to help motivate the participants to achieve their goals. One year later, physical activity in the group had increased by an average of 487 calories per week with exercises of moderate intensity, the equivalent of adding five brisk 1-mile walks per week. After 2 years, the exercisers were still burning an average of 445 more calories a week compared with levels before the start of the program.

Even disabled people can turn their activity levels around. A clinical trial involving more than 200 sedentary, disabled older people, ages 60 through 94, tested a home-based strength training program. The program started out with a home visit in which exercisers viewed a motivational tape on the benefits of exercise and potential obstacles to exercise, they set goals and received exercise instruction on how to use elastic bands for strength training. A second, reinforcing home visit 3 weeks later was followed up by an average of 7-8 phone calls between the exercise group and health professionals over the 26 weeks of the study. At the end of 6 months, a high proportion of the older people — some 78 percent — stuck with the exercise program. In this group, function greatly improved and

OLDER PEOPLE MAY BE ABLE TO EXERT MORE CONTROL OVER THEIR OWN HEALTH THROUGH IMPROVED COMMUNICATIONS WITH PHYSICIANS AND OTHER CLINICIANS.

overall disability declined by about 18 percent. This study is one of several conducted at the NIA-supported Edward R. Roybal Centers for Research on Applied Gerontology. The Centers are designed to move promising social and behavioral research findings in a number of areas — exercise, computer skills, driving ability, caregiving, nursing home care — out of the laboratory and into programs that can help improve the lives of older people and their families.

One way older people may also be able to exert more control over their own health is through improved communication with physicians and other clinicians. Research by scientists supported by NIA, as well as the pharmaceutical industry, is trying to open a window into what happens in the doctor's office when it comes to discussing medications. One recent study of communications about over-the-counter (OTC) medications followed 414 patients of 27 doctors. Some 58 percent of the patients in the survey said they discussed the use of these types of medications with their physicians. Doctors asked about OTC use in only 37 percent of the patients' visits. Researchers suggest that more might be done on both sides to encourage discussions about OTC medications so that patients can become more active partners in the management of their medicines.

Along these lines, the NIA has published two award-winning guides, one for patients and the other for clinicians. The companion publications, *Talking with Your Doctor* and *Working With Your Older Patient*, have been widely distributed, and they are among the most requested of NIA's public information materials. Both publications can be viewed on NIA's website. Printed copies of *Talking with Your Doctor* are also available from NIA's Information Center. See the back of this booklet for contact information.

As research continues to explore the role that individual capabilities and attitudes play in health and age, it is critical to understand population issues as well. Each of us is part of a larger world of public and social institutions — the health care system, Federal, state, and local government, and other private and public agencies — that can have a direct affect on aging, health, and retirement.

As the population ages, the ability to characterize demographic trends and understand what is behind them will become increasingly important. A number of studies are underway that should help inform policymakers and others in addressing the aging of society.

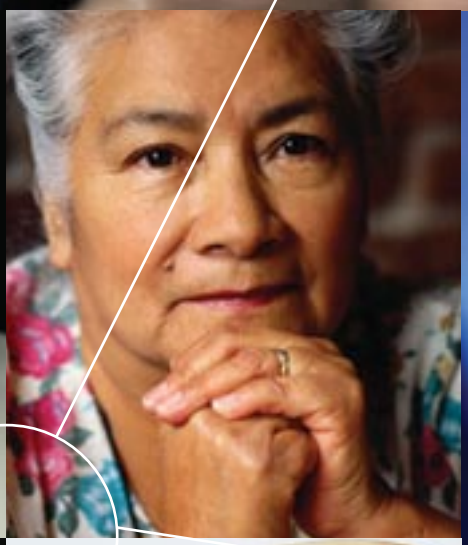
A most basic question, of course, is how long will we live. As biologists and geneticists search for the molecular and cellular secrets of aging, population studies by NIA-supported demographers provide new and compelling evidence that median life span in industrialized countries is increasing, and at an accelerated rate. A recent examination of Swedish national demographic data from 1861 through 1999, provides the longest available series of reliable information on extreme old age in the world. The data show that the maximum age at death during the time studied rose from 101 to 108. Before 1969, the pace of the increase was .44 years per decade; it accelerated to 1.1 years per decade after 1969. According to researchers, reductions in death rates at older ages are responsible for the increase in life span in Sweden and in other industrialized countries over the last few years. These trends, they say, seem likely to continue and may gradually extend the limits of human longevity even further.

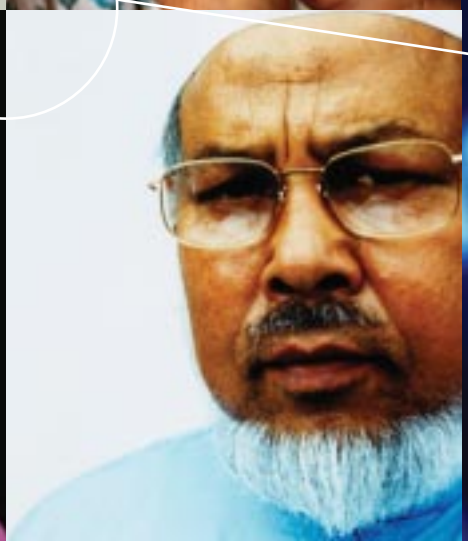
While we are living longer, we are also living better. Researchers were surprised by recent studies finding that, at the same time longevity was increasing in the U.S., disability rates among older Americans were declining. Since these analyses of data from the National Long-Term Care Survey were first presented in the early 1990s, the reduction in the rate of disability has accelerated, suggesting that older people in the U.S. are functioning better than they have in more than a decade. This is true even for the most vulnerable among us, people age 85 and older. In fact, the most recent findings from this research suggest that the reduction in disability may even be keeping older people out of nursing homes. From 1992 through 1999, the study showed a 22 percent drop — some 200,000 people — in the number of people in nursing homes, a finding that has broad implications for how society might address a possible increase in the need for long-term or nursing home care as the baby boom ages. "The challenge now," says Dr. Suzman, "is to find ways to maintain or even improve the trends in disability amid a steep rise in the number and proportion of older people."

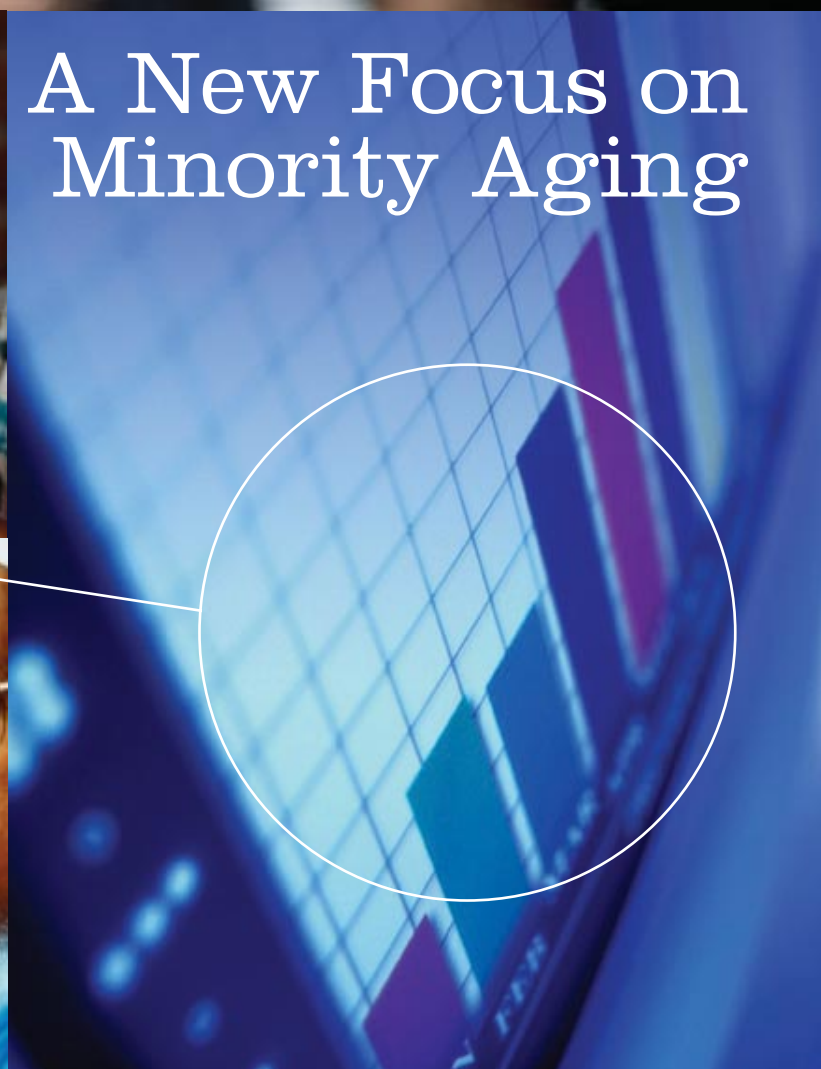
A NUMBER OF STUDIES ARE UNDERWAY THAT SHOULD HELP INFORM POLICYMAKERS AND OTHERS IN ADDRESSING THE AGING OF SOCIETY.

Health Disparities

A New Focus on Minority Aging







Health Disparities

A New Focus on Minority Aging

The racial and ethnic makeup of the U.S. is changing, and the older population is no exception. It will become significantly more diverse in the coming years, a shift that has potentially broad implications for an aging society and for aging research. And while the health of racial and ethnic minority groups has improved steadily in recent years, disturbing disparities persist among racial and ethnic groups.

Demographic projections show that the older population will look dramatically different over the next few decades. This increasing diversity comes amid growing recognition of differences in health status and life expectancy among racial and ethnic groups.

In 1997, for example, average life expectancy at age 65 was 16.1 years for African Americans and 17.8 years for non-Hispanic whites. In general, surveys indicate, African American, American Indian, and Hispanic ethnic and racial groups are disadvantaged relative to whites on most indicators of health and disease, while Asian Americans appear to be as healthy, if not healthier. There are important differences among ethnic subgroups as well.

Studies so far on racial and ethnic differences in health suggest that a complex assortment of factors may be at work. Disease risk, diagnosis, progression of disease, response to treatment, caregiving, and overall quality of life are all affected by a number of important variables, including race, ethnicity, gender, socioeconomic status, age, education, occupation, country of origin, and perhaps other lifetime and lifestyle differences. "Understanding these relationships will require a thoughtful program of research," says Dr. J. Taylor Harden, NIA Assistant to the Director for Special Populations.

A major effort is already underway. In 1994, NIA established its Resource Centers on Minority Aging Research (RCMARs) to study health status, health practices, and interventions for improving the health of older minorities. The RCMARs also are charged with training and recruiting minority scientists into the field of aging research. In addition to the RCMARs, NIA also supports and conducts a wide range of related research. These studies have looked at menopause, osteoarthritis, cardiovascular disease, cognitive function and Alzheimer's disease (AD), diabetes, demographic and social factors, and physical frailty.

Some important insights are beginning to emerge. One major effort, the Study of Women's Health Across the Nation (SWAN), follows the natural history of menopause in a large multi-racial and ethnic sample of women, age 40 through 55. Initial baseline findings from the study show that the reporting of specific menopausal symptoms, from hot flashes and night sweats to forgetfulness, varied

WHILE THE HEALTH OF RACIAL AND ETHNIC MINORITY GROUPS HAS IMPROVED STEADILY, DISTURBING DISPARITIES PERSIST AMONG RACIAL AND ETHNIC GROUPS.

significantly among racial, ethnic, and socioeconomic groups and by lifestyle. Scientists point out that research in this area may ultimately be able to help provide guidance to clinicians in assessing symptoms by increasing their sensitivity to racial and ethnic differences in reporting menopause symptoms.

One area of increased attention is AD. Some studies have shown that Hispanic and African Americans may have a higher overall risk of AD than do whites. Other reports are mixed. NIA is most interested in examining the diagnostic tests for AD to evaluate whether a diagnosis of AD is affected by racial, ethnic, cultural, or educational factors. These tests, which measure abilities in language, memory, and cognitive function, may be more difficult in general for people from some cultures and ethnic groups than others, in ways that are not related to a diagnosis of dementia. NIA is working with the research community to improve the validity and reliability of AD diagnostic testing across different groups.

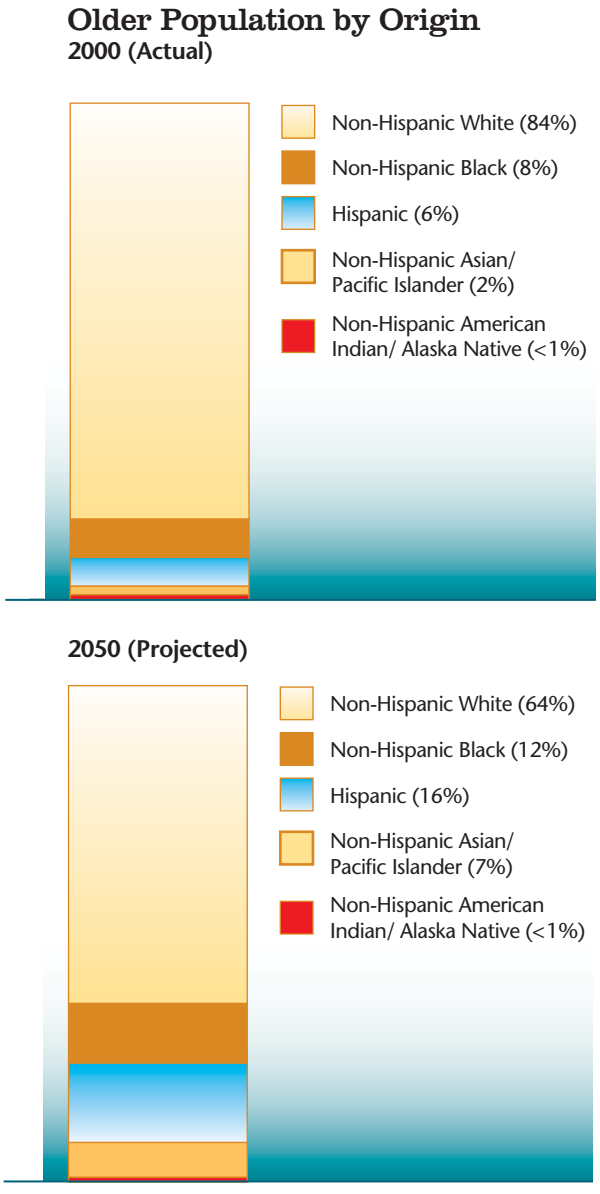
In the coming years, the Institute seeks to do more. The *NIA Strategic Plan to Address Health Disparities in Aging: Fiscal Years 2000-2005*, provides guidance, calling for three major areas of focus: 1) research to advance understanding of health disparities in age-related disease, with the goal of developing new and improved approaches for detecting, diagnosing, preventing, delaying, or treating disease; 2) development of a research infrastructure to train researchers and support institutions conducting health disparities research; and 3) using public information, outreach, and education to increase public awareness of health disparities and transfer what has been learned to health professionals.

Several new initiatives are planned. Among them is an innovative effort by scientists at NIA's Intramural Research Program to rethink how studies are conducted in minority communities and how minorities and socioeconomically disadvantaged groups can be included in health and aging research. This new paradigm, or model, of research on minority aging includes development of a Medical Research Vehicle (MRV) for conducting age-related studies in the community. The 47-foot customized semi-trailer includes 3 working areas: an examination room with a

blood donor station; a cardiovascular fitness and muscle strength testing area; and a bone density/body composition and vascular studies testing area. The state-of-the-art vehicle is often used in conjunction with a community center or other facility, where administrative activities of the study and other research, such as cognitive and neuropsychological testing, can be done.

The MRV has been used in the pilot phase of the newly initiated Healthy Aging in Nationally Diverse Longitudinal Samples (HANDLS) study. The study's major goal is to help understand the role of socioeconomic status in the development of age-associated disease and disability. This research will place special emphasis on cardiovascular disease, cerebrovascular disease, age-associated changes in cognition, strength and physical functioning, and body composition, as well as other areas in which health disparities have been identified. Recruitment strategies will be examined to identify the most culturally appropriate, cost-effective and efficient approaches for participation of minorities and medically underserved populations and will specifically look at the effectiveness of the MRV for these studies. "We hope that the recruitment strategy, if successful, could serve as a model for development in other studies that require an ethnically and socioeconomically diverse group of participants," says Dr. Michele Evans, Deputy Scientific Director of the Intramural Research Program and Principal Investigator of the HANDLS study.

STUDIES ON RACIAL AND ETHNIC DIFFERENCES IN HEALTH SUGGEST THAT A COMPLEX ASSORTMENT OF FACTORS MAY BE AT WORK.



Source: U.S. Census Bureau

For More Information

PUBLICATIONS

NIA offers a wide variety of free publications. *Age Pages* are short fact sheets on many different topics. Public information also includes booklets about exercise, menopause, anti-aging therapies, and doctor-patient communication, as well as resource directories for women's health and aging services. You can order publications from the NIA Information Center, by calling toll free or by writing:

NIA Information Center
P.O. Box 8057
Gaithersburg MD 20898-8057

Toll free telephone: 1-800-222-2225
Toll free TTY: 1-800-222-4225

WEBSITE

The NIA website offers information to the public, health professionals, and researchers about the institute and its programs. Most of the NIA's publications are available online. Researchers can find out more about grant and training opportunities as well. You can visit the NIA website at:

http://www.nia.nih.gov

ALZHEIMER'S DISEASE (AD)

The NIA's Alzheimer's Disease Education and Referral (ADEAR) Center can send you publications about AD symptoms, diagnosis, and treatment. Information specialists also can provide referrals to supportive services and organizations, as well as referrals to research facilities or the nationwide network of NIA-funded Alzheimer's Disease Centers. The ADEAR website has publications, a calendar of events, and a bibliographic database as well as a list of Federally-funded clinical trials on AD. You can contact ADEAR online, by calling toll free, or by writing:

ADEAR Center
P.O. Box 8250
Silver Spring, MD 20907-8250

Toll free telephone: 1-800-438-4380
Website: www.alzheimers.org
E-mail: adear@alzheimers.org

MEDIA INQUIRIES

Resources for the media are available through the NIA's Office of Communications and Public Liaison (OCPL).

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