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Record Group/Collection: George H.W. Bush Presidential Records
Collection/Office of Origin: Speechwriting, White House Office of
Series: Speech File Backup Files
Subseries: Chron File, 1989-1993

OA/ID Number: 13665
Folder ID Number: 13665-002

Folder Title:
Dedication, Alzheimer's Center 4/27/89 [OA 6263] [1]

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(Lange/Wallace)
April 25, 1989
3:00 p.m.
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PRESIDENTIAL REMARKS: DEDICATION, ALZHEIMER'S CENTER
PALM HARBOR, FLORIDA
THURSDAY, APRIL 27, 1989
1:50 P.M.

((Thank you, Mike [Congressman Bilirakis]... You know, in a little town near here, a guy got the attention of the local fish and game warden. Seems he brought in a huge catch, every time he went out on the lake. So the warden asks if he can go along with him, the next time. The guy says, "Sure."

So they get out there in the boat early one morning, and the guy reaches into his tackle box, pulls out a stick of dynamite, lights it, and throws it over the side. There's a big explosion under water -- and a dozen fish float to the surface.

The warden yells at him, "Don't you know that's illegal?" Well, the guy reaches down, pulls out another stick of dynamite, lights it, hands it to the warden, and says, "You want to argue? Or you want to fish?"))

Well, you didn't send anyone to Washington to argue. Or to fish -- although I do love fishing in the warm waters of the Florida coast. No, you sent us to Washington to find solutions. And Congressman Bilirakis has been finding solutions and support for Alzheimer's patients. For his work, we are all grateful.

It's a special honor to be here, on behalf of a cause that matters so deeply, to so many. Alzheimer's Disease extracts a devastating toll on its victims -- and on those who love them. By the time this century ends, more than one out of four Americans will be over 50 -- and will face some risk of being striken with this disease.

The Michael Bilirakis Alzheimer's Center is the first facility in the nation designed to care for Alzheimer's patients -- all the way from diagnosis, to caring for them in their final days. This center will serve as a place of hope, and a source of comfort, until a cure is found.

While the disease may ravage its victims, it makes heroes and heroines of all who care for them. And while it challenges the very fabric of the family, it also demands new strength -- a strength in each other, that we might not have known we had.

But above all, this disease is a reminder of what ought to be an American birthright: that we should be able to live out our lives as engaged, productive, and full participants in this community of citizens.

In a nation that looks after its own, that birthright entails its own responsibility: That any definition of a successful life must include serving others. That success is not, cannot, be measured by the sum of our possessions, but by the good we do for others. That whatever life, and health, and love we have within us, we must share with others.

Older Americans represent a phenomenal reserve of talent and experience -- qualities this country can use right now. So even as I join you in dedicating a place of refuge and comfort for those stricken with a deadly disease, I would ask all of you who have the health and inclination, to consider how much we gain, when we give of ourselves.

In New York City, my wife Barbara met with a group helping young Cambodians learn English. While she was there, one older lady told Barbara how desperately lonely she had been, before she volunteered. Her eyes filled with tears at remembering it. And then her face lit up, as she told Barbara, "I've never been lonely a day since."

One person's need matches another's -- and a wonderful thing happens. I always like to remember that there is no exercise better for the human heart than reaching down, and lifting someone else up. The rest of your life really should be the best of your life.

At the Inaugural, I spoke of a new engagement in the lives of others. Today, I challenge those of you who can, to get involved -- and stay involved. Find a place, or an organization, or even a single life, where you can make a difference for someone else.

So many of you already have. Some of you do volunteer work at local hospitals -- or in one of the constellation of community groups in and around Palm Harbor. I understand a number of the men here have been helping boys in trouble, at the Sheriff's

Youth Ranch. And many of you at St. Mark's are donating your time to help out on the Alzheimer's unit.

To those of you who are making the lives of the less fortunate a little easier, I offer my admiration -- and my thanks.

"The young know the rules," Oliver Wendell Holmes once said; "but the old know the exceptions." Many of you already <u>are</u> exceptions -- and exceptional. And I cheer you on.

Thank you. God bless you. And God bless America.

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National Institute on Aging
Special Report on Alzheimer's Disease: 1988

For the past 15 to 20 years, scientists have been making steady, but slow progress in the battle against Alzheimer's disease. This past year, their efforts came together to produce several important advances in this field--generating excitement in the scientific and medical communities, as well as among the general public. In the space of a few months time, scientists announced the prospects for new inroads into understanding of the genetics of the disease, and a potential treatment for some of its most serious symptoms.

Research on Alzheimer's disease is supported or conducted by the National Institute on Aging (NIA), the National Institute of Neurological and Communicative Disorders and Stroke (NINCDS), the National Institute of Allergy and Infectious Diseases (NIAID), the National Eye Institute (NEI), and the Division of Research Resources (DRR).

How Prevalent is Alzheimer's Disease?

Although the exact number is not known, it is estimated that between 2.5 and 3 million Americans--including more than 8 percent of the U.S. elderly population--suffer from Alzheimer's disease. These estimates are based on numerous studies, many of which only include data for institutionalized populations. Little is known about the prevalence of Alzheimer's disease in the community where some four-fifths of all older people with dementia may live.

There is little consistency among studies that examine the full range of dementia in its mild, moderate, and severe stages. Many reasons exist for the wide range of estimates reported up to this time, including: 1) lack of agreement on diagnostic tests, particularly for early stages of disease, 2) lack of consistency in the way tests are administered, 3) differences in populations studied, and 4) inadequate testing due to the high cost of conducting a thorough examination.

To overcome some of these obstacles and to develop a clearer picture of the prevalence of Alzheimer's disease, the NIA supports research aimed at standardizing the diagnosis of Alzheimer's disease and measuring the very subtle behavioral changes that are the first signs of disease. Efforts to develop standardized instruments and approaches to detect the earliest stages of dementia will help to assess the true magnitude of this disorder.

One example of data that differ markedly from those of previous reports is found in a recent study of the residents of East Boston, Massachusetts. This 3-year NIA-supported study

conducted by Dr. Denis Evans and his colleagues at Harvard University in Boston has revealed an unexpectedly high rate of dementia in this population.

The study was designed to determine the extent of confusion and forgetfulness in noninstitutionalized persons over age 65 living in East Boston. Approximately 3,800 people participated in the study. The scientists found rates of mild impairment as high as 18.7 percent, with an additional 9.08 percent of the population suffering from moderate and 3.07 percent from severe impairment. Further, more than one-half of all persons over age 85 in this community had some degree of dementia. These rates are two to three times those reported in most earlier studies.

The researchers found that the rates of Alzheimer's disease and other forms of cognitive impairment rose markedly with age. Remarkably, however, more than 80 percent of the impairment appeared to be caused by Alzheimer's disease--much higher than the 40 to 60 percent previously estimated.

It is unclear what these high prevalence rates mean; until more is known, the investigators urge that the findings be interpreted cautiously. NIA scientist Dr. Lon White offers several potential explanations, including the possibility that findings related to individual communities may be influenced differently by such variables as genetics, the environment, or a myriad of sociocultural factors such as the propensity to care for sick persons at home rather than in institutions.

Ongoing studies may shed light on the reasons for this unusual and unexpected finding.

Advances in Molecular Genetics

The earliest reports of research on Alzheimer's disease suggested that at least some cases of the disease are inherited. In the 1960's and 1970's, Alzheimer's disease was first linked to Down syndrome, the genetic disorder caused by abnormalities on chromosome 21. Since that time, scientists pursuing clues on the possible causes of Alzheimer's disease have suggested that it might run in some families.

Now, scientists supported by NIA and NINCDS have reported that a gene may be responsible for the 10 to 30 percent of Alzheimer cases that seem to be inherited, and that this gene may play a role in sporadic (or nonfamilial) cases, as well.

Led by Dr. Peter St. George-Hyslop at the Massachusetts General Hospital in Boston, Massachusetts, scientists affiliated with a dozen research institutions announced that they had found a gene responsible for production of amyloid protein, a pathological "marker" associated with Alzheimer's disease. The amyloid protein gene is located on chromosome 21 adjacent to the region associated with Down syndrome. (This work was

accomplished in part with support from the NIA Alzheimer's Disease Research Center program.)

The investigators pooled information from four families living in the United States, Canada, West Germany, Italy, and France. In each of the families, there were a large number of Alzheimer cases and an autosomal dominant pattern of inheritance; in other words, offspring of an Alzheimer patient had a 50 percent chance of developing the disease.

The investigators then employed sophisticated techniques of molecular genetics first developed at the Massachusetts General Hospital and since utilized to begin mapping genetic defects in Huntington's disease, cystic fibrosis, and various chronic diseases long thought to have some genetic component. This technology uses chemical substances called restriction enzymes to cut long chains of DNA (the molecular basis of all inherited characteristics) into smaller segments. Over the past few years, investigators have developed a number of these restriction enzymes which recognize particular patterns along the DNA chain and cut it at specific points. If the DNA is even slightly altered, the enzyme will not make the cut. In this way, scientists are able to trace how specific segments of genetic material are inherited.

Although an Alzheimer's disease gene has not yet been fully isolated, the work by Dr. St. George-Hyslop and his colleagues gives scientists an opportunity to find out more about the role of genetics in causing Alzheimer's disease. Because of the similarities between the rare familial and the more typical sporadic cases of Alzheimer's disease, this work may also tell us something about Alzheimer's disease in the general population.

While there is much work ahead, scientists are encouraged by the long-term possibilities of presymptomatic diagnosis of Alzheimer's disease, at least in severely affected families. Should a successful treatment be developed, early intervention may be key to halting or delaying the progress of the disease.

Cloning the Amyloid Gene

As the search goes on for an "Alzheimer gene," scientists are using advances in molecular genetics to study other basic changes that take place in the brains of Alzheimer patients. Earlier this year, a great deal of excitement was generated by news that a team of NINCDS and other NIH scientists had successfully cloned a normal human gene involved in making amyloid. (This is discussed more fully in the NINCDS section of this report.)

Much of the progress in this area has been possible because the gene that directs the production of amyloid is active in the human heart, lungs, and muscles, in addition to brain tissue. The fact that the gene and its product, amyloid, could be found

outside the brain made it more accessible to study.

Recently, NIA grantee Dr. Charles Marotta and his colleagues at the Harvard Medical School demonstrated that the amyloid gene can be cloned directly from brain tissue of deceased Alzheimer patients--bringing us one step closer to understanding the basic changes that take place as Alzheimer's disease develops.

This work is an extension of earlier studies in which Dr. Marotta and his colleagues first showed that messenger RNA can be studied in autopsied brain tissue. RNA is a key chemical in the production of protein, a process that is critical to the life of the cell. Dr. Marotta's team found that if the autopsied brain has been stored under routine laboratory conditions, RNA will continue to synthesize protein as if in a living brain, even years after death.

In recent studies, Dr. Marotta examined postmortem brain tissue from four individuals--two Alzheimer patients (67 and 88 years old) and two neurologically healthy individuals (73 and 79 years old). In the last of these four cases, the investigators looked at brain tissue that was prepared using a new rapid autopsy procedure that permits examination of the tissue within hours after death.

Dr. Marotta found that, in many instances, the amount of RNA remains sufficiently stable after death to allow intricate studies of genes and their products. This research not only contradicted other studies that reported a decrease in RNA either prior to or following death of Alzheimer patients, but confirmed that such work could be accomplished using autopsy tissue prepared under routine conditions.

This development allows further study of Alzheimer's disease by sophisticated molecular genetics techniques that may eventually reveal the cause of this debilitating illness.

A Need for Further Research

Shortly after the news that scientists had located the amyloid gene on chromosome 21, French scientists announced yet another advance in our understanding of the genetics of Alzheimer's disease. Working in collaboration with NINCDS scientists, Dr. Jean Maurice Delabor at the Laboratorie de Biochimie Genetique in Paris announced that patients who suffer from sporadic Alzheimer's disease, as well as certain types of Down syndrome patients, have an abnormal number of copies of the gene that produces amyloid: three instead of two. In both groups of patients studied, the abnormal gene duplication occurred on the same critical segment of chromosome 21. These findings strengthen the evidence of a genetic defect in Alzheimer's disease, and may explain the long-suspected link between Alzheimer's disease and Down syndrome. (Down syndrome patients, if they live long enough, often develop Alzheimer's disease

symptoms.) Scientists now seek to confirm these findings, to learn why having three copies of the amyloid gene might result in Alzheimer's disease or Down syndrome, and to uncover other abnormal ways this gene is expressed in Alzheimer patients.

Most recently, NIA-supported scientists trying to replicate this work announced that they had failed. According to Dr. Dennis Selkoe and his colleagues at Brigham and Women's Hospital in Boston, none of 14 Alzheimer patients in their study had more copies of the amyloid gene on chromosome 21 than did the 12 non-demented aged individuals whom they studied. The 14 patients included those with and without a family history of Alzheimer's disease.

In view of these findings, further studies of the amyloid gene on chromosome 21 and of the process that results in production of abnormal amounts of amyloid in patients with sporadic or familial Alzheimer's disease are needed.

The mixed results of this past year have pointed the way to some answers about the genetics of Alzheimer's disease. Further studies are needed to look at other segments of chromosome 21 and perhaps other chromosomes as well. In the meantime, it is important to note that the use of state-of-the-art biotechnology has made possible and has stimulated increased interest in the study of the basic nature of Alzheimer's disease.

A Unique Population for Genetic Research

One difficulty in genetic studies of Alzheimer's disease is that pooling data from different families may skew the results by mixing information about various forms of the disease. Recently, Dr. Thomas Bird and colleagues at the NIA-supported Alzheimer's Disease Research Center at the University of Washington in Seattle, have identified a population group that might resolve this problem and, in turn, answer some of the questions that have been raised about the location of the Alzheimer gene.

The scientists are studying five Volga German families, all of whom descend from persons who once lived in two small Russian villages. More than 50 members of these five families have suffered from Alzheimer's disease in a typical autosomal dominant pattern. Perhaps more importantly, what the investigators found strongly suggests that Alzheimer's disease has been transmitted through as many as four generations from a single common ancestor.

In the mid-18th century, several thousand Germans moved to Russia to farm the lands along the Volga River. They came at the invitation of Catherine the Great, herself a German, who promised them freedom to retain their cultural identity in return for their willingness to settle land that had historically been over-run by marauders and invaders. Until the 20th century, when the Volga Germans came under attack by the new Russian government,

they did just that, intermarrying exclusively among themselves. During World War I, a large number emigrated to the United States and have since become known to researchers as a unique cultural group.

Dr. Bird and his colleagues hope to look more closely at the Volga Germans and analyze the suspect areas of chromosome 21. If, indeed, this unique population shares a single genetic predisposition to Alzheimer's disease, the investigators may be able to confirm or refute Dr. St. George-Hyslop's findings regarding an Alzheimer gene.

Research on Other Possible Causes

As early as 1976, investigators working with Alzheimer patients discovered a link between the disease and aluminum. Since that time, numerous studies have confirmed an increase of 10 to 30 times the normal concentration of aluminum in the brains of individuals who have died with Alzheimer's disease. Yet scientists still don't know the exact role that aluminum plays in the development of the disease or how aluminum enters the human brain.

This year, two NIA grantees reported their findings on how aluminum can gain access to the brain, despite its protection by the blood-brain barrier and the fact that aluminum is not readily absorbed by the digestive system.

Drs. Daniel Perl and Paul Good at the Mt. Sinai Medical Center in New York City, found in animals that aluminum can be transported directly into the brain from the nasal passages, along the olfactory pathway.

In their study, Drs. Perl and Good placed a small amount of spongy material saturated with an aluminum solution into the nasal passages of rabbits. Within a month, the animals developed abnormalities in those portions of the brain that involve the sense of smell. While not identical to the changes seen in Alzheimer's disease, these abnormalities nonetheless occurred in areas of the brain that are affected by the disease.

Although aluminum is the third most prevalent element in the earth's atmosphere--and people are exposed to it through airborne dust--the animals were exposed to levels that far exceeded the norm. In future experiments, Drs. Perl and Good will be looking at the effect of lower levels of exposure, more like those found in the environment.

At the University of Alabama in Birmingham, Dr. Richard Jope has found new evidence supporting the controversial notion that aluminum in the diet may be responsible for brain cell death. Dr. Jope found that high concentrations of aluminum in the drinking water of laboratory rats can alter the vital balance of calcium within brain cells. Since the primary role of calcium is

to initiate the full range of activities that keep the cell alive, this can have a major effect on brain functioning. Furthermore, Dr. Jope found that aluminum alters energy metabolism in the cell by offsetting the balance of two chemical messengers (cyclic AMP and cyclic GMP). This balance is another important factor in determining normal cell metabolism and function.

Toward a Treatment for Alzheimer's Disease

In November, 1986, California-based physician William K. Summers announced that an experimental drug called tetrahydroaminoacridine (THA) appeared to reduce memory loss in a small group of Alzheimer patients. The announcement generated a flood of articles in the news media along with a public outcry for access to this new "miracle drug." This past year, one NIA-supported scientist took steps to validate and expand Dr. Summers' preliminary results while a second grantee looked at the effect of the drug on experimental animals to determine how, and if, the drug might work.

In a clinical trial that began in August 1987, a group of independent investigators from 17 research facilities across the country are measuring the safety and efficacy of THA by testing it in approximately 300 Alzheimer patients. This study is designed to take place over 2 years under the leadership of Dr. Kenneth Davis, Director of the NIA-supported Alzheimer's Disease Research Center at the Mount Sinai School of Medicine in New York City, and is the result of a joint effort of the NIA, the Alzheimer's Disease and Related Disorders Association, and the Warner Lambert Company.

Memory loss is perhaps the major disabling symptom of Alzheimer's disease. In the early stages of the disease, the patient becomes more and more forgetful--neglecting to turn off the oven, misplacing things, rechecking to see if a task was done, taking longer to complete a previously routine chore, or repeating already answered questions. As the disease progresses, a patient loses the ability to remember places, time, close relatives and friends, and sometimes even his or her own name.

Several experimental treatment approaches have focused on correcting deficits in acetylcholine, the chemical messenger that helps control memory. But acetylcholine is only one of several neurotransmitters affected by Alzheimer's disease; other brain changes cause mood and behavior problems, disorientation, loss of judgment and ability to concentrate, and eventually loss of motor function. Experts in the field have been cautiously optimistic about THA's potential as a treatment, largely because the drug's action seems limited to increasing acetylcholine levels.

In recent experiments at the University of California at Irvine, Dr. Carl Cotman and his colleagues have found that THA might have an effect on brain cells that goes beyond its effect

on acetylcholine. The scientists took samples of brain tissue from the hippocampus (memory control center) of guinea pigs, applied THA to the tissue, and found that the drug stimulated cell activity. This work may help to explain the apparent improvement that Dr. Summers observed in some Alzheimer patients.

Diagnosing Alzheimer's Disease

NIA intramural scientist Dr. Jay Luxenberg and his colleagues have developed a method which may help to identify patients in the early stages of Alzheimer's disease, and predict how rapidly the disease will progress.

Using computed tomography (CT), a radiologic technique which produces images of the brain's anatomy, the researchers have found that serial CT scans, performed at six month intervals, can distinguish dementia from normal brain aging. While CT is widely used in the diagnostic evaluation of patients with memory impairment, its value has been limited to identifying tumors and focal lesions from stroke, injury, or other neurological conditions. In this study, the scientists used computers to measure the volume of the brain's ventricles (fluid-filled spaces). Previous research using CT to calculate ventricular size had given them baseline data on Alzheimer patients as compared to normal, healthy control patients.

The research team found that progressive ventricular enlargement occurs in dementia, that it is detectable in as short a time as six months, and that the rate of ventricular enlargement correlates with the rate of cognitive decline.

Because the symptoms and course of Alzheimer's disease vary from individual to individual, serial CT scans may be particularly useful in separating mild, slowly progressive dementia from the more rapidly progressive type that typically occurs in the rare familial form of Alzheimer's disease. In future studies, NIA scientists will attempt to determine whether this technique can be used to study other progressive dementing illnesses.

National Institute of Neurological and Communicative Disorders and Stroke

As the principal supporter of neurologic research in the United States, the National Institute of Neurological and Communicative Disorders and Stroke is extensively involved in the study of Alzheimer's disease. NINCDS scientists and grantees are pursuing basic studies of brain and brain cell abnormalities associated with this dementing illness, and in clinical investigations are seeking methods for earlier, more precise diagnosis.

Further Progress in Molecular Genetics

One of the most intriguing recent discoveries in Alzheimer's disease research comes from the NINCDS laboratories of Dr. Dmitry Goldgaber and Nobel laureate Dr. D. Carleton Gajdusek. In collaboration with scientists from the National Cancer Institute, the NINCDS scientists reported cloning a normal human gene involved in making amyloid, the substance found in high concentrations in the characteristic plaques of the brains of Alzheimer patients, and mapping the gene's location to human chromosome 21. These reports opened the search for a genetic defect that could predispose people to Alzheimer's disease. Finding such a defect might lead to a diagnostic tool for identifying people at risk for Alzheimer's.

A study by another NINCDS scientist, Dr. Ronald Polinsky, has shown that chromosome 21 is involved in Alzheimer's disease. This year he and other U.S. and European scientists reported finding several families in which Alzheimer's disease is caused by an autosomal dominant gene defect; the defect was traced to chromosome 21. His finding and those that preceded it allow scientists to narrow their focus to that one chromosome.

Detailed family trees developed by NINCDS grantee Dr. Nancy S. Wexler at the Hereditary Disease Foundation in Los Angeles have been used to develop markers for chromosome 21. Originally compiled to trace Huntington's disease in Venezuela, these pedigrees have served as a standard reference to chromosome 21 genes. The markers developed will make it possible for scientists to examine more accurately the relationship between Down syndrome and Alzheimer's disease.

PET Studies

Family trees are useful in identifying familial Alzheimer's disease, but other tools are necessary when the disease occurs sporadically. Positron emission tomography (PET), a technique that depicts the rate at which glucose is metabolized (used) in the living brain, is one such tool helping research scientists distinguish Alzheimer's disease from other conditions that cause dementia.

Guided by PET images, NINCDS scientist Dr. Thomas Chase has

been able to divide patients with primary degenerative dementia into two groups based upon the location of the metabolic deficiency in the brain: anterior dementia and posterior dementia. He found that anterior dementia, which is less common and is characterized by prominent personality and social or behavioral changes, may overlap with another neurologic disorder called Pick's disease.

Also drawing on information gained from PET studies, Dr. David Kuhl, an NINCDS grantee at the University of Michigan in Ann Arbor, showed that while the rate at which glucose is metabolized in the brain may be the same for patients with and without Alzheimer's disease, the pattern of metabolism is different. The studies of Drs. Chase and Kuhl add new elements to our understanding of the abnormal brain function in patients with Alzheimer's disease.

Risk Factors and Treatments

Scientists do not know what causes nor what could prevent Alzheimer's disease but they are exploring all areas that may yield answers. One such area focuses on neurotransmitters, the naturally occurring chemicals that ferry messages from nerve cell to nerve cell. Low levels of certain neurotransmitters have been linked to Alzheimer's disease, the most consistent abnormality being a reduction of the neurotransmitter acetylcholine. Diminished levels of norepinephrine and somatostatin have also been reported in Alzheimer patients.

Dr. Thomas Chase recently reported further evidence of a link between neurotransmitters and Alzheimer's disease symptoms. He found that intellectual impairment corresponded to reduced levels of somatostatin in the cerebrospinal fluid of Alzheimer patients. Dr. Chase has begun clinical trials of the drugs clonidine, tetrahydroaminoacridine (THA), and a synthetic somatostatin (SMS) to replace or enhance the diminished neurotransmitters norepinephrine, acetylcholine, and somatostatin.

According to one theory, Alzheimer's disease may result from a loss of trophic factors, which are naturally occurring substances that help nerve cells make and maintain appropriate connections. NINCDS grantee Dr. Bruce Wainer, studying the role of trophic factors in Alzheimer's disease at the University of Chicago, has found in tissue culture that one of these factors, nerve growth factor, can prevent the degeneration of certain nerve cells in the brain after they have been damaged. Further research may point to a specific relationship between nerve growth factor and Alzheimer's disease.

In related studies, Dr. Wainer has shown that some cell lines he has cultivated demonstrated the capacity to group together and develop, rather than divide as cells most often do. These results shed more light on nerve survival,

regeneration and growth--all important mechanisms in nerve repair.

National Institute of Allergy and Infectious Diseases

As the brain gradually degenerates in Alzheimer's disease, areas that have died leave holes in the once solid mass, giving the brain a spongy appearance. This transformed structure is not unlike that seen in a few other rare degenerative brain diseases --including kuru and Jakob-Creutzfeldt disease in humans and scrapie in sheep and goats--caused by "slow viruses" or other "unconventional" virus-like agents. The similarities among these brain diseases have led some researchers to investigate whether Alzheimer's disease might be caused by a virus or other agent.

Scrapie as a Model for Alzheimer's Disease

Scrapie research is of particular interest to researchers investigating Alzheimer's disease, which has no animal model. The changes in the brain seen in scrapie--the genesis of large tangles of nerve fibers and clumps of dying nerve cells--in some ways mirror those seen in Alzheimer's disease; thus the causative agents of these two diseases or their methods of wreaking destruction may be similar.

At the NIAID Rocky Mountain Laboratories in Hamilton, Montana, Dr. Richard E. Race and colleagues are trying to identify and unravel the biochemistry of the infectious scrapie agent. Evidence gathered so far indicates that it is like a virus except in two important ways: it evades the immune system and has no detectable genetic material.

Because efforts to isolate the scrapie agent from animal tissue have been unsuccessful, Dr. Race and colleagues have been trying to develop a laboratory system that yields large quantities of infected cells. They already had succeeded in growing the scrapie agent in a cell line derived from mice, but the yield of infected cells in each culture was very low, only one to two percent. To increase this level, they recently separated out the infected cells and, through a laboratory technique called cloning, made multiple copies of them. Cultures of cloned cells contain 50 to 100 times more agent than the culture from which the original cells were derived. This system provides a new source of homogenous scrapie agent that will enable extensive biochemical studies of the agent.

Considerable controversy surrounds the nature of the scrapie agent. One proposed candidate is called the prion protein (PrP), a molecule containing a high percentage of protein and lacking any genetic material. Tissue samples of scrapie infectivity contain large amounts of PrP. Dr. Race and colleagues have been examining PrP and its relation to disease; to test its possible infectivity, they inoculated the protein into the brains of weanling mice. All mice given PrP are still alive and show no signs of disease 330 days after inoculation, whereas after 180

days, all mice in a control group inoculated with cells infected with scrapie were dead. The scientists conclude that PrP is not likely to be the infectious scrapie agent but more likely is a normal cellular protein that becomes altered and accumulates as a result of the disease process. This work further confirms that of NIA grantee Dr. Stanley Prusiner of the University of California at San Francisco, who originally proposed that the prion protein breaks down in normal cells, but for some reason remains intact in infected cells.

Alzheimer's Disease--A Quirk of the Immune System?

Supported by NIAID and NIA, Dr. Roy L. Walford of the University of California at Los Angeles has reviewed what is known about the immunological aspects of Alzheimer's disease and has proposed two theories for how a specific genetic variant of one "player" in the immune response may influence the development of sporadic Alzheimer's disease. It previously had been found that sporadic Alzheimer's disease (which, unlike familial Alzheimer's disease, does not have a clear-cut genetic link) has a high degree of association with this genetic variant.

Dr. Walford's theory focuses on a crucial element of a healthy immune response called complement, a series of about 25 proteins that "complement" the action of antibodies, proteins that defend the body against infection. The complement system works in an amplifying cascade: activation of the first component (C1) triggers activation of the second component (C2), which triggers activation of a third component, and so on in the manner of concentric circles caused by a rock thrown into a pool of water.

People with sporadic Alzheimer's disease have been found to have one particular genetic variant of the fourth component of complement much more often than any other variant; this variant is called C4B2.

Dr. Walford offers two theories on why this might be significant. The first proposes that because complement is vital to the removal of infected cells, C4B2 may represent a defective complement component that increases one's susceptibility to neuronal damage. That is, C4B2 may prevent complement from doing its part in clearing nerve cells infected with a virus or virus-like agent or damaged by an environmental toxin.

Alternatively, C4B2 may represent a defective complement component that allows an inherent imbalance in the aging immune system to be accentuated. High levels of autoantibodies, proteins that attack one's own tissues, have been observed in healthy individuals; studies in mice show that the number of these autoantibodies increases with age. When the number of autoantibodies overwhelms the immune system's ability to counteract them, some autoantibodies evade the immune system's defenses and thereby destroy tiny areas of brain tissue. This

process together with normal hardening of arteries in the brain, which also kills small numbers of nerve cells, is thought to account for the expected but symptomatically minor neurological damage that occurs in the normal aging brain. In people with the C4B2 variant, however, these processes may accelerate to the point where nerve cell death becomes so extensive that it causes dementia. This may occur, Dr. Walford says, because C4B2 is less effective than other variants of C4 at keeping nerve cell destruction in check.

Division of Research Resources

Each year scientists conduct thousands of research studies at General Clinical Research Centers (GCRC), which operate in major U.S. research medical centers with funding from the NIH Division of Research Resources. These centers provide flexible clinical research facilities for both inpatient and outpatient studies, as well as the specialized personnel and laboratories needed by investigators funded by other components of NIH, other Federal and state agencies, and private foundations. The centers constitute the major source of extramural NIH support for research with patients.

New Diagnostic Approaches

Several GCRC studies have found evidence that Alzheimer's patients may have biochemical abnormalities in addition to the decreases in acetylcholine discussed earlier in this report. The interpretations of these results, however, are difficult. It is not known, for example, whether the abnormalities are a cause or an effect of the disease. Also, there are often substantial overlaps in the data obtained from normal aged subjects and Alzheimer patients.

At the Massachusetts Institute of Technology GCRC in Cambridge, DRR- and NIA-supported grantees Drs. Suzanne Corkin and John Growdon have found that an enzyme present in the cerebrospinal fluid was lower in concentration in patients with Alzheimer's disease than in healthy age-matched subjects. Low levels of this chemical called butyrylcholinesterase correlated with dementia, memory impairment and language disorder. Although there was some overlap in the values obtained from the two groups of patients, the results suggest that the enzyme level may serve as a marker for some behavioral abnormalities associated with the Alzheimer's disease. However, the specificity of this potential marker must be established through further research.

Currently, Alzheimer's disease is diagnosed by excluding other possiblities. A variety of cognitive tests are required. Factors such as the patient's motivation and ability to communicate adequately can interfere with such test results. Drs. Patricia N. Prinz and Michael V. Vitiello, grantees at the University of Washington GCRC in Seattle, examined the potential

usefulness of sleep patterns and changes in EEG (a measure of the brain's electrical activity) as possible diagnostic and prognostic indicators for early Alzheimer's disease.

They observed increased wakefulness, decreased deep sleep, and marked slowing of EEG, as well as loss of power in certain frequency bands of the EEG, among Alzheimer's patients while they were awake and asleep. Using these parameters, the GCRC investigators achieved at least an 85-percent-accurate classification of Alzheimer's disease based on clinical criteria in a group of healthy and affected subjects. The researchers hope that eventually biological markers such as the ones they are testing can be exactly characterized so that data might be obtained with home monitors and later analyzed. These biological markers may ultimately aid in the diagnosis of patients.

Further Evidence of a Genetic Defect

Expanding on the earlier mentioned link between Alzheimer's disease and Down syndrome, researchers at the Johns Hopkins Outpatient GCRC are examining patients with Down syndrome to gain a better understanding of the disease process. Jointly funded by DRR and NIA, Drs. Marshal Folstein, Andrew C. Warren and other grantees at the Hopkins GCRC believe they have found a correlate of Alzheimer's disease among the 60 community-dwelling subjects who visit the GCRC outpatient clinic every 6 months.

The researchers have found that some people with Down syndrome over the age of 40 tend to show significant symptoms of behavioral and global cognitive decline characteristic of Alzheimer's disease. The study of these and other similarly affected subjects promises to improve the understanding of how Alzheimer's disease occurs, according to the research team.

Outlook

This past year, the National Institute on Aging took a major step in establishing research on Alzheimer's disease and the neuroscience of aging as high priority areas with the creation of two new organizational units: the Office of Alzheimer's Disease Research and the Neuroscience and Neuropsychology Program.

The Office of Alzheimer's Disease Research will coordinate the many Institute activities on Alzheimer's disease from within the Office of the NIA Director. The Neuroscience and Neuropsychology program will serve as one of three extramural research programs. One of the first initiatives of staff in the new program was to establish a special group of awards for Leadership and Excellence in Alzheimer's Disease (LEAD). The LEAD award will provide stable support (up to 7 years with up to $1 million per year) to outstanding senior scientists in the field.

The Institute's Information Office took steps toward the establishment of a national Alzheimer's Disease Education Center by: 1) awarding a contract to assess the public's information needs, and 2) convening a national planning conference bringing together scientific, health care, social service and lay experts in this area. The goal of the Center will be to provide accurate, timely information on the disease, its consequences, potential treatments, new research and available services to the millions who are touched by this disease.

In addition to the type of research highlighted in this report, the NIA also continued its support for studies on helping families to cope with this devastating disease. New initiatives for the coming year include increased support for studies of family caregiving, the start-up of international studies designed to determine risk factors for Alzheimer's disease by examining the incidence of the disease among various populations, and expansion of the Institute's Alzheimer's Disease Research Center program.

NIH's programs on Alzheimer's disease are aimed at better diagnosis, care, and treatment for the 2.5 to 3 million Americans who suffer from this disease.

National Institute on Aging

Age Page

Senility: Myth or Madness?

"Senility"—something which most of us fear in old age—is not a normal sign of growing old; in fact, it is not even a disease.

Rather, "senility," or the medical term "dementia," describes a large number of conditions with an equally large number of causes, many of which respond to prompt treatment.

The symptoms of dementia include serious forgetfulness, confusion, and certain other changes in personality and behavior. While doctors and patients alike used to routinely dismiss these symptoms as incurable effects of old age, they are not necessarily. Nor are small memory lapses in old age a sign of "senility." Slight confusion or occasional forgetfulness throughout life may only signify an overload of facts in the brain's storehouse of information.

Diagnosis

The two most common incurable forms of mental impairment in old age are multi-infarct dementia and Alzheimer disease (pronounced altz'hi-mer). Multi-infarct dementia is caused by a series of minor strokes which result in widespread death of brain tissue. This condition accounts for about 20 percent of the irreversible cases of mental impairment. In Alzheimer disease changes in the nerve cells of the outer layer of the brain result in the death of a large number of cells. Some 50 to 60 percent of all older persons with mental impairment have Alzheimer disease.

Some 100 reversible conditions may mimic these disorders. A minor head injury, a high fever, poor nutrition, or adverse drug reactions, for example, can temporarily upset the normal activity of extremely sensitive brain cells. If left untreated, such medical emergencies can result in permanent damage to the brain, and possibly even death.

In much the same way, emotional problems can be mistakenly confused with irreversible brain disease. Depression, loss of self-esteem, loneliness, anxiety, and boredom can become more common as older persons face retirement, the deaths of relatives and friends, and other such crises—often at the same time.

Persons suspected of having Alzheimer disease or multi-infarct dementia should have thorough physical, neurological, and psychiatric evaluations. This includes a complete medical exam, as well as tests of the patient's mental state, and highly specific tests such as the brain scan. The brain scan is useful in that it can rule out a curable disorder. The brain scan may also show signs of normal age-related changes in the brain, such as shrinkage, which are not necessarily a sign of disease.

The patient plays an important role in the diagnosis by giving information on past medical history, the use of drugs—both prescription and over-the-counter—diet, and general health. Because part of the medical exam depends

(over, please)

upon how much a patient is able to remember about past events, the doctor may also ask a close relative for information.

Treatment

The best treatment comes only after a complete medical examination by one who does not dismiss complaints as "just old age." If there is a diagnosis of a curable disease, the doctor will know how to treat it or will have ready access to the best resources or specialists.

If the diagnosis is one of the irreversible disorders, there is still much that can be done to treat the patient and to help the family cope. Careful use of drugs can lessen agitation, anxiety, and depression, and improve sleeping patterns if this is needed. Proper nutrition is particularly important, although special diets or supplements are usually not necessary. The person should be encouraged to maintain daily routines, physical activities, and social contacts, and should not be discouraged from trying new things. Often, stimulating the individual—by supplying information on the time of day, place of residence, and what is going on in the immediate environment and in world events—encourages the use of skills and information which remain. This in turn may keep brain activity from failing at a more rapid pace. In the same way, providing memory aids helps people help themselves in day-to-day living. Such aids can include a very visible calendar; list of daily activities; written notes about simple safety measures; and directions to, and labeling of, commonly used items.

In any event, a patient with an irreversible disorder should be under the care of a physician. This may be a neurologist, psychiatrist, or family physician, internist, or geriatrician—who is willing to devote the time and interest required to closely watch treatment; to treat the physical and emotional problems that may complicate the course of the disease; and, of course, to answer the many questions that the patient and family may ask.

There are many differences in the type, seriousness, and order of changes in cases of irreversible dementia. Even so, there is enough similarity in the experiences of patients and their families—the loneliness, the frustrations, the lack of information and resources for good medical care—to have led to the development of family groups around the country. The Alzheimer's Disease and Related Disorders Association (7 East Lake Street, Chicago, IL 60601; phone, 800-621-0379 or 800-572-6037 in Illinois), which has more than 100 chapters across the country, encourages research, education, and family services.

Prevention

Diet, drugs, and lifestyle may someday be used to prevent or reverse the damage done to the brain in Alzheimer disease and other related diseases. At the present time, however, our understanding of these problems and their causes is just beginning to unfold.

Developing interests or hobbies and becoming involved in activities which keep the mind and body active are among the best ways that older people can avoid the problems which can mimic irreversible brain disorders. Careful attention to physical fitness, including a balanced diet, may also go a long way towards keeping healthy. There appear to be certain physical and mental changes which occur with age even in healthy persons, but in the long run, much pain and suffering can be avoided if older persons, their families, and their physicians realize that "senility" is not part of aging.

Reprinted February 1986

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES Public Health Service National Institutes of Health

☆U.S. Government Printing Office: 1986—491-280/20015

National Institute on Aging
Special Report on Alzheimer's Disease: 1987

Among the many disorders associated with growing older, Alzheimer disease is one of the most devastating and most feared. Alzheimer disease causes a variety of physical, psychological and emotional changes; the final stages of the disease are marked by a complete loss of memory and, as one author recently described it, a loss of self. In addition to the toll it takes on those who suffer from it, Alzheimer disease presents enormous problems to patients' families and raises complex social and economic issues for society. At the National Institutes of Health, Alzheimer disease presents a unique challenge to scientists who are trying to find out what causes the disease, how it progresses, and how we can treat, cure and maybe someday prevent it.

Alzheimer disease is no longer regarded--as it was only a decade ago--as a natural consequence of aging. It does, however, affect a substantial proportion of older people. Although exact numbers are not known, it is estimated that between 2.5 and 3 million people have Alzheimer disease, and that the total cost of their care adds up to nearly $90 billion each year.

The risk of developing Alzheimer disease increases as people grow older. More than one-half of all the people who have ever survived to age 65 are alive today, and as many as one of every 10 has Alzheimer disease. A large number of older people alive today will survive to age 85, when their chances of developing Alzheimer disease may be one in three. Because of the growth of the older population, and the particularly rapid growth of the population over age 85, the number of people with Alzheimer disease is expected to quadruple by the middle of the 21st century.

At the National Institutes of Health (NIH), the National Institute on Aging (NIA) is the primary focus for research on Alzheimer disease. Research on it is also conducted or supported by the National Institute of Neurological and Communicative Disorders and Stroke (NINCDS), the National Institute of Allergy and Infectious Diseases (NIAID), the National Eye Institute (NEI), and the Division of Research Resources (DRR).

Diagnosis Using Abnormal Brain Proteins

One of the major challenges facing scientists is the diagnosis of Alzheimer disease. More than three-quarters of a century ago, Alois Alzheimer identified the disease by looking at autopsied brain tissue. Even today, the only way to diagnose the disease definitely is to examine brain tissue after a patient's death. Several recent and very significant findings, however,

may soon lead to a chemical test for diagnosing Alzheimer disease.

At the Albert Einstein College of Medicine in the Bronx, New York, NIA grantee Dr. Peter Davies has discovered an abnormal protein (A-68) in the brains of Alzheimer patients, particularly in those areas most severely affected by the disease. To locate this specific protein, Dr. Davies and his colleagues developed a monoclonal antibody called Alz-50. Antibodies, which are produced by the body's immune system as a means of fighting disease, bind to corresponding molecules in much the same way as a key fits a lock; monoclonal antibodies, which can now be produced in the laboratory, can be designed so that they will locate and bind to specific molecules in body tissue.

Using Alz-50 as a probe, the New York investigators found abundant amounts of A-68 in the brains of each of the more than two dozen Alzheimer patients that they tested. The largest concentrations were found in the brain's cortex, or outer layer, as well as the more deeply placed hippocampus. Both the cortex and the hippocampus are vital to memory and other mental functions and both are severely damaged in Alzheimer disease.

Although Dr. Davies found A-68 throughout the diseased nerve cells, most of it was concentrated in the degenerating nerve cell endings that form the characteristic neuritic plaques of Alzheimer disease. The protein's location, coupled with information on its weight, solubility and other characteristics, distinguish it from proteins in normal brain tissue and other proteins recently identified in Alzheimer tissue.

Most recently, the scientists found A-68 in the cerebrospinal fluid of nine patients with presumptive diagnoses of Alzheimer disease, and in none of six healthy individuals. If this work is corroborated by others, it may allow diagnosis through lumbar puncture. If A-68 is found in the blood of Alzheimer patients, it could lead to an even more valuable diagnostic tool.

These studies may also reveal more about the mechanisms of brain cell death in Alzheimer disease. In a small percentage of the Alzheimer samples he studied, Dr. Davies found A-68 in apparently healthy cells. The investigators speculate that these cells may later develop the damage typical of Alzheimer disease and that the presence of the protein may signal an early stage in the disease's destructive process.

The Tau Protein in Neurofibrillary Tangles

In related studies at the Institute for Basic Research in Developmental Disabilities in Staten Island, New York, NIA grantee Dr. Henryk Wisniewski and his colleagues have found another brain protein that plays a role in Alzheimer disease. In this case, the protein is a normal one that is altered in the

diseased brain.

Dr. Wisniewski's research focuses on the chemical origin of neurofibrillary tangles (twisted nerve cell fibers) which, like plaques, are hallmarks of Alzheimer disease in autopsied brain tissue. Dr. Wisniewski and his colleagues have found that the normal protein "tau" is a major component of neurofibrillary tangles.

In the healthy cell, tau is the building block of microtubules. Microtubules are tiny cylindrical structures made up of long strands of protein that help transport nutrients and other substances between the body of the nerve cell and its terminals. In the affected cells of the Alzheimer brain, the hair-like strands of protein that make up microtubules become twisted into neurofibrillary tangles. Dr. Wisniewski's findings now suggest that some change in the tau protein causes the fibers to tangle, which in turn disrupts the normal transport system, and eventually leads to cell death.

The researchers are hopeful that the identification of the modified tau protein might eventually lead to a test for Alzheimer disease. In fact, they have already developed antibodies that react with substances in the cerebrospinal fluid which bathes the brain. They are even more excited by the possibilities of identifying what may be one of the earliest changes to take place in the Alzheimer brain.

Studies by grantees of both the NIA and the National Institute of Neurological and Communicative Disorders and Stroke (NINCDS) are already confirming Dr. Wisniewski's findings. At Brigham and Women's Hospital in Boston, Massachusetts, Drs. Dennis Selkoe and Kenneth Kosik have shown that Alzheimer disease is associated with massive reorganization of the microscopic structures within the cell body. Like their New York colleagues, these investigators speculate that the tau protein is largely responsible.

Several years ago, Dr. Selkoe and his colleagues developed an antibody to investigate the twisted fibers that make up neurofibrillary tangles. At that time, he and his colleagues speculated that the tangles were composed of highly stable proteins unlike any found in healthy brain cells.

In their most recent experiments, the investigators looked at the microtubules whose role is so critical to the life of the cell. They, like Dr. Wisniewski, found abnormal accumulations of tau interferring with the finely regulated transport system in the cell body.

Neuropsychology and the Diagnosis of Alzheimer Disease

Until a chemical test for Alzheimer disease becomes available, physicians and researchers will continue to use

standard clinical examinations and new, more sophisticated neuropsychological tests. At Harvard University, NIA grantee Dr. Marilyn Albert and her colleagues have developed a test which they say may be very sensitive to the changes that occur in Alzheimer patients' memories.

The test is more like a game than any of the standard neuropsychological tests in current use. The person administering the test shows the subject a disc applied to a board, then covers the board and applies a second disc to another area of the board. The board is then uncovered and shown to the subject once again, who is asked to identify the new disc. In some variations of the task, the discs are blank (to test the subject's memory for spatial relations); in other variations, the discs are imprinted with words (to test verbal memory). The subject can use any means at all, even pointing, to identify the new disc and thus complete the task.

The value in terms of diagnosis comes when the test is repeated 15 seconds and then 2 minutes later. According to Dr. Albert, Alzheimer patients have considerable memory loss after 2 minutes. Even patients who suffer severe memory loss of Korsakoff's syndrome, a form of dementia associated with chronic alcoholism, do not forget as much information in the one minute and 45 seconds between the two tests.

The test is quick and easy to administer; it is practical for both research and clinical settings; and it can be modified to test patients of vastly different educational levels. Perhaps most importantly, it presents virtually no threat to individuals concerned about their abilities to perform on a memory test.

Dr. Albert and her colleagues have examined several thousand patients with tentative diagnoses of Alzheimer disease, Huntington's disease, and Korsakoff's syndrome. They hope to learn more about the accuracy of their test after autopsy examination permits a definitive diagnosis.

Positron Emission Tomography: A Promising Diagnostic Tool

Advances in the use of positron emission tomography (PET) may make it more valuable in detecting Alzheimer disease than once thought. Early studies with PET, which is a safe, non-invasive method for viewing metabolic activity in the living human brain, showed reduced metabolism in particular parts of the cortex in Alzheimer patients. This discovery was useful in explaining the various symptoms of the disease. However, until recently, PET was considered to be of limited diagnostic value since it detected metabolic changes only in patients in advanced stages of the disease.

New research conducted by NIA intramural scientist Dr. James V. Haxby and his colleagues suggests that PET may detect neurological changes in less severe cases of Alzheimer dementia,

opening the possibility of earlier interventions to control the disease. Dr. Haxby found patients with mild dementia to have impaired metabolism in particular regions of the brain. Instead of being uniformly distributed over the cortex, the abnormalities appeared to predominate in either the left or right hemisphere of the brain. Moreover, at later stages of the disease, the affected region corresponded to the patients' ability to perform certain tasks on a test of mental abilities.

PET detected these abnormalities in the earliest stages of Alzheimer disease, when clinical diagnosis remains uncertain because symptoms are limited to impaired memory. While memory loss is often the first symptom of dementia detected by a physician, it may be the result of any number of causes, many of which are reversible. Although PET technology is still limited to a few medical centers, it may aid clinicians in differentiating between Alzheimer disease and these other conditions. Under the direction of Dr. Robert P. Friedland, NIA will conduct follow-up studies to confirm its usefulness.

Mechanisms of Alzheimer Disease

In the 1970's, it was clearly established that Alzheimer disease causes a serious decrease in the neurotransmitter acetylcholine, one of several chemical messengers in the brain, and one that is closely tied to memory and other mental functions. This finding stimulated considerable scientific activity aimed at identifying the exact nature of the defect and finding a way to treat the disease with drugs, in much the same way as Parkinson's disease is treated. However, Alzheimer disease now appears to be too complex a problem, involving many different elements of brain chemistry and anatomy, for this approach.

Dr. Donald Price, who heads the NIA-supported Alzheimer Disease Research Center at the Johns Hopkins University in Baltimore, Maryland, has found that Alzheimer disease disrupts the chemical messengers involved in memory, thinking, mood, arousal and response as well as in chemicals that stimulate and control these activities. His latest research suggests that there is also a reduction of corticotropin-releasing factor (CRF) in parts of the Alzheimer brain. CRF is the hormone that activates the adrenal gland and initiates the body's response to stress.

This is the first time that CRF has been linked to Alzheimer disease, and it may explain the depression that frequently accompanies Alzheimer disease. Dr. Price will continue to study various neurotransmitters and other brain chemicals that play a role in the symptoms and progression of this disease.

The Calcium Connection

One area that has captured the excitement of the scientific

community--and may eventually make it possible to piece together much of what is known about Alzheimer disease--involves the delicate balance of calcium concentrations within the brain.

The primary role of calcium within nerve cells is to transmit information and initiate the full range of activities that keep the cell alive and the brain functioning. In the healthy brain, the normal level of calcium within the cell is as much as 100,000 times less than that outside the cell. When the cell is stimulated, the level of calcium increases temporarily and sets cell activity in motion; thereafter excess calcium in removed. If the concentration of calcium remains high in the cell for too long, the cell dies.

Independent studies by NIA grantees Drs. Gary Gibson (Burke Rehabilitation Center, White Plains, New York), Gary Lynch (University of California, Irvine), Mary Michaelis (University of Kansas, Lawrence), Philip Landfield (Wake Forest University, Winston-Salem, North Carolina), Ralph Nixon (McLean Hospital, Belmont, Massachusetts), and Dean Smith (University of Wisconsin, Madison) all point to disruptions in the vital balance of calcium in Alzheimer disease and, to a much lesser extent, in normal aging. Most recently, scientists have speculated that excess calcium in nerve cells may be the key to changes in brain metabolism, neurotransmitter activity, protein production, transport of vital nutrients, and perhaps the entire range of changes that scientists see in the Alzheimer brain.

Towards a Treatment for Alzheimer Disease

Research on the mechanisms of Alzheimer disease has clearly established one thing--nerve cells die, particularly in that part of the brain that commits information to memory. Now, an NIA-supported scientist at the University of California, Irvine has found that surviving brain cells make a futile attempt to hold off the ravages of cell death.

Several years ago, Dr. Carl Cotman and his colleagues demonstrated that a nerve cell whose connections to other nerve cells was severed by a sudden injury or accident could "resprout" new nerve fibers so that the brain's circuitry was not disturbed. Now he has shown that the brain also tries to compensate for the steady nerve cell loss seen in such chronic conditions as Alzheimer disease.

The investigators compared brain tissue from patients who had died with Alzheimer disease with tissue from individuals of the same ages who had died of various causes. In the Alzheimer tissue, they found that brain cell death stimulated compensatory growth of new connections, or axons.

Whether these new connections help restore lost function in the brain, or simply add to the confusion, is not known. Nonetheless, the investigators are hopeful that it may someday be

possible to exploit the brain's natural, albeit limited, ability to repair itself.

Management of the Alzheimer Patient

Many, although not all, Alzheimer patients wander either during the night or intermittently during the day and night. In hospitals and nursing homes, this means that nurses must monitor the patients one-on-one to keep them from hurting themselves. In the home, wandering is just one more stress added to the already demanding load on caregivers.

At the National Institutes of Health Clinical Center, NIA and hospital staff have developed a practical solution to this problem by using a device that looks like an ordinary wristwatch. Designed by Horace Cascio and George Hemphill, with the help of head nurse Kathleen Musallam and her staff on NIA's six-bed unit, the monitoring device consists of a wristwatch case equipped with a very low power radio transmitter. As the patient walks through the unit, the watch sends out a signal. If the patient comes within 6 feet of either of the unit's two exits, the signal is picked up by radio receivers mounted above the ceiling tiles near the door. The signal is then transmitted to a computer located at the nurses' station, triggering an alarm and alerting staff that a patient is about to leave the unit.

Staff are very enthusiastic about the monitoring system which protects patients from environmental hazards without being constrictive. They also feel that, with little or no modification, the system might be used to track the movements of individuals in nursing homes and other long term care facilities, hospitals and day care centers. According to Ms. Musallam and her colleagues on the hospital's administrative staff, the system is in the final stages of development and testing.

Help for Alzheimer Patients at Home

Many people believe that home is often the most supportive place for an Alzheimer patient. As Alzheimer disease progresses, however, even the home can become an unfamiliar--and sometimes threatening--environment.

In order to help both patients and their families, a team of NIA-supported scientists from the University of Washington in Seattle is studying the changing physical and mental abilities of Alzheimer patients over time, and the growing challenges that they face in their own homes as a result.

For several years, Dr. H. Asuman Kiyak and her colleagues have been studying Alzheimer patients and their families at home. The investigators are looking at the patients' physical health--including changes in their abilities to see, hear, and walk; the patients' mental health--including failing memory and awareness of time; and their needs and preferences in terms of

such things as privacy and security. They then evaluate this information in terms of the basic physical characteristics of each house, including the floor plan, stairs, lighting, and the number of clocks, calendars, and complex electrical appliances.

Although the 3-year study will not be completed for another year, the investigators report some interesting preliminary results. Not surprisingly as the disease progresses, Alzheimer patients find it increasingly difficult to operate microwave ovens, vacuum cleaners, light switches, dishwashers, and other electrical appliances. Families also report that patients experience problems with heat and cold, often becoming frustrated in their attempts to adjust room or water temperatures.

Rather than making changes in the house layout or routines, however, most families simply deal with problems as the occur. This often means assuming responsibilities that the patients can no longer handle, thus adding to the already overwhelming burden on the person responsible for care.

Dr. Kiyak and her colleagues feel that it may be necessary, and far less difficult for the family, to simplify the patient's physical environment. The investigators hope that their final results will offer some practical solutions to helping patients and families at home.

National Institute of Neurological and Communicative Disorders and Stroke

As the principal source of support for neurological research in the United States, the NINCDS is vitally involved in the study of Alzheimer disease. NINCDS scientists are pursuing basic studies of brain and brain cell abnormalities associated with this dementing illness. At the same time, clinical investigators are trying to improve the diagnosis of Alzheimer disease, which can be mis#aken for other neurological disorders. To accomplish these goals, neuroscientists use sophisticated brain imaging and laboratory techniques.

Tangling with Brain Proteins

This year, NINCDS-supported investigators found abnormalities in the distribution of proteins within neurons that contain neurofibrillary tangles.

Dr. Donald Price--whose research on Alzheimer disease was discussed earlier in this report--and Dr. Ludwig Sternberger at the University of Maryland School of Medicine in Baltimore are independently studying the proteins that make up neurofilaments. This year, working separately, both scientists found an abnormality in an important biochemical process called phosphorylation. This process, in which phosphate is added to protein, regulates the activity of many of the body's enzymes, and these in turn control basic physical processes such as tissue growth. Although phosphorylation normally takes place in the axon, Drs. Price and Sternberger found that in Alzheimer patients, phosphorylation occurs in the cell body. In this abnormal location, phosphorylation may alter the physical properties of the neurofilaments, perhaps increasing their rigidity.

More on the Calcium Connection

NINCDS grantee Dr. Michael Shelanski at New York University Medical Center in New York City has found unusually low calcium levels in skin cells obtained from Alzheimer patients. The patients' levels were 70 percent less than those found in healthy older people and 81 percent less than those in healthy young people. These striking differences in calcium levels between patients and healthy people may enable scientists to use the levels of calcium in skin cells to design a new diagnostic test for Alzheimer disease. Moreover, in view of these preliminary findings, Dr. Shelanski suspects that brain cells of Alzheimer patients may similarly show abnormalities in calcium levels.

Infectious Proteins

Some scientists have suggested that Alzheimer disease might be caused by a "slow virus" infection that lies dormant in the body for many years before producing symptoms. This year,

NINCDS/NIA grantee Dr. Stanley Prusiner of the University of California at San Francisco, who previously coined the term "prion" for an unusual infectious particle associated with some slow virus disorders, identified a gene in mice that controls the incubation time of scrapie, a slow viral disorder first described in sheep and goats. Dr. Prusiner found that different strains of miche developed scrapie after differing lengths of time. Analysis of the mice's genetic material revealed that both the prion protein gene and the gene that controls the incubation period, the "clock gene," are on the same chromosome. This close genetic link means that the prion protein gene can serve as a marker for the clock gene, making it possible to identify the strain of mice most likely to get the disease first.

This is the first evidence of a genetically controlled biological clock in animals that times or triggers the development of a disease.

Dr. Prusiner hopes to use the prion protein gene to study timing mechanisms in human neurological disorders such as Alzheimer disease. If a similar linkage between a prion protein gene and a clock gene can be found in the chromosomes of people with Alzheimer disease, scientists may have an explanation as to why most cases of the disease occur after age 65.

Helping Nerve Cells Make Connections

According to one theory, Alzheimer disease may result from a loss of important substances, called trophic factors, that help nerve cells make and maintain appropriate connections with other nerve cells. NINCDS/NIA grantee Dr. Bruce Wainer at the University of Chicago in Illinois has found new evidence that nerve growth factor (NGF), a protein known to be important in the function of peripheral nerves, may be one of several trophic substances that aid the survival of cholinergic nerve cells in the brains of patients with Alzheimer disease. When Dr. Wainer added NGF to cultures of nerve tissue from mice embryos, the substance caused the nerve cells in culture to mimic the normal growth process of the cells in the brain: The cells in culture sent out extensions or fibers that connected with other cells. NGF also helped the nerve cells survive in culture. Further research may point to a specific relationship between NGF and Alzheimer disease.

Brain Imaging

Imaging brain metabolism with PET is helping scientists identify similarities and differences between Alzheimer disease and other dementing neurological disorders. PET studies conducted first at the University of California in Los Angeles and now at the University of Michigan in Ann Arbor by NINCDS grantee Dr. David Kuhl showed that the abnormal metabolic pattern in the brains of patients with Alzheimer disease is remarkably similar to the metabolic pattern seen in patients with

Parkinsonian dementia. Additional research may show that a similar mechanism causes the cognitive decline in both disorders.

Dr. Kuhl also reported that PET scans of patients with multi-infarct dementia (dementia caused by many small strokes) show abnormalities over a wider area of the brain than do the PET scans of Alzheimer patients. This finding may help physicians develop diagnostic guidelines to better distinguish between these two types of dementia.

This year, NINCDS/NIA grantees Dr. Marek-Marsel Mesulam at Beth Israel Hospital in Boston, and Dr. Martin Reivich at the University of Pennsylvania in Philadelphia further defined a new disorder that is similar to Alzheimer disease but less debilitating. The new disorder, known as slowly progressive aphasia without generalized dementia, involves a gradual loss of language function over time but neither loss of memory nor aberrant social behavior.

The investigators found that the PET scans of people with slowly progressive aphasia differed markedly from those of Alzheimer patients. In patients with the newly identified disease, metabolism was reduced in the language area of the left hemisphere; patients with Alzheimer disease had relatively more global abnormalities. This finding may help scientists recognize new dementing disorders of later life with a different prognosis than Alzheimer disease, and may eventually lead to the development of distinct approaches to prevention and treatment.

National Institute of Allergy and Infectious Diseases

Scientists have observed that physical abnormalities in the brain associated with Alzheimer disease are similar to those of the slow virus disease scrapie, which is the focus of several studies supported by the National Institute of Allergy and Infectious Diseases (NIAID). Like Alzheimer disease, scrapie is characterized by the appearance of porous or sponge-like areas in the brain. Autopsies reveal large fibrous structures and neurologic plaques whose cause is unknown. Because of these similarities, and also because Alzheimer disease does not occur in animals, scrapie may make a good research model for studying human dementias, such as Alzheimer disease and a rare, but transmissible fatal brain disorder known as Creutzfeldt-Jakob disease.

A Possible Model for Alzheimer Disease

NIAID intramural scientists Drs. Bruce Chesebro, Richard Race, Jerry Keith, and Camille Locht are currently studying the prion protein, described earlier in this report, in hopes of determining its relationship to the infectivity of scrapie. This past year, Dr. Chesebro and his colleagues determined the complete genetic sequence for the gene coding for the prion protein made in mice. This gene was found to be very similar to the corresponding gene in hamsters.

To facilitate more detailed studies of scrapie, Dr. Race and his colleagues adapted the scrapie agent isolated from infectious animals so that it would grow in test tubes. They successfully grew the scrapie agent in cultured mouse cells, which were rigorously tested to be sure that the infectious agent was indeed present and active. The researchers found that even though the cells remained infectious, after a time the prion protein itself could not be isolated. The scientists further noted that infection was species-specific: mouse scrapie agent grew in mouse-derived cells, while the hamster scrapie agent did not.

To study the infectious agent further, Dr. Race and his associates now hope to increase the amount of agent infecting each cell, as well as to increase the number of infected cells in each cell culture.

By elucidating the genetic structure of the scrapie agent, and also improving the model in which it can be studied, this research is providing information that may ultimately help in the understanding of Alzheimer disease.

Conclusion

During the coming year, research on Alzheimer disease will continue to develop in many scientific areas as NIH scientists and grantees look for answers as to the prevalence, incidence, cause, course, treatment, management, cure and possible prevention of Alzheimer disease.

Studies on the prevalence of Alzheimer disease will investigate the fascinating suggestion that the disease is three times more common among Americans than among Japanese. To do this, NIA scientists hope to collaborate with Japanese investigators in examining data from studies in the U.S. and Japan, and to initiate a new study of Japanese-Americans in Hawaii.

A national registry of Alzheimer patients will be established. In September 1986, the NIA awarded funds to six grantees who will determine the best ways to diagnose and follow the course of persons with Alzheimer disease, and thus develop a better idea of the extent of this public health problem.

NIH will also continue to fund research on the causes of the disease, and on risk factors that might be modified. Some of this research will be supported through NIA's Alzheimer Disease Research Center program which currently supports 10 specialized centers across the country. Another focus will continue to be the social aspects of the disease, with the goal of providing useful information for relatives, friends, health professionals and other caregivers.

In the area of health education, NIA will begin work toward establishing a national Alzheimer Disease Education Center. The Center's goal will be to provide accurate, timely information on the disease, its consequences, potential treatments, new research and available services to the millions who are touched by this disease.

All of NIH's efforts are aimed at better care for the 2.5 to 3 million Americans who suffer from Alzheimer disease and the millions more who face the possibility of developing this disease in the future.

DIFFERENTIAL DIAGNOSIS OF DEMENTING DISEASES

National Institutes of Health
Consensus Development
Conference Statement
Volume 6 Number 11
July 6-8, 1987

Introduction

Dementia in the adult population is a major and growing medical and social problem. It occurs at all ages but increases with advancing age, so that the largest group of demented patients is in the older age groups. Dementia has its highest rate in the population over age 75, the age group that is increasing at a higher rate than any other. Recent scientific advances give promise of major increases in knowledge and skills that will result in better diagnostic tests and better methods of treatment.

Dementia, because it interferes with the dignity and independence of the person, causes widespread suffering, not only for the person affected but also for families, friends, and caretakers. The expense of long-term care, either at home or in a nursing facility, can be overwhelming: It has been estimated at $40 billion a year for people age 65 and older.

Proper identification of the disease state responsible for dementia in the individual patient is critical to management. Some diseases that produce dementia can be arrested or reversed (e.g., benign mass lesions of the brain, intoxication, infections, and metabolic and nutritional disorders). Some dementing diseases are infectious, and the tissues and bodily fluids require special handling to prevent transmission. Some dementing diseases are inherited, and this has important social and ethical consequences. The value of therapeutic trials for dementia that are now in progress, and of the epidemiologic studies of prevalence and incidence under way in delineated populations, is limited by the criteria and accuracy of diagnosis.

It is important to distinguish the early stages of dementia, the clinical behavioral state, from the nonprogressive cognitive changes known to occur in otherwise normal aging. This is not always possible. Serial examination of the patient over a period of time is still the best way to do this. Neuropsychological tests have been developed, and efforts continue to refine them so that dementia can be identified and distinguished from other mental states that may be confused with it. It is important to identify the specific pathological state that produces dementia in the individual patient. The usual clinical methods for doing this are sufficient for certain conditions. Brain-imaging methods and biochemical and genetic markers have advanced a long way and show a stunning promise for the future.

At the present time, diagnoses of many of the important dementing diseases can be confirmed or denied with certainty only at autopsy. Pathological diagnosis is the standard of accuracy of clinical diagnosis. Very few of the dementing diseases can be studied in an animal model. Pathological studies, while monitoring clinical diagnosis, are providing new knowledge that can be expected to lead to effective antemortem diagnosis of dementing diseases that are now indiagnosable while the patient is alive.

In an effort to assess the current state of knowledge about the differential diagnosis of the dementias, the National Institute on Aging, the National Institute of Neurological and Communicative Disorders and Stroke, and the National Institute of Mental Health in conjunction with the NIH Office of Medical Applications of Research convened this conference. Following 1-1/2 days of presentations by experts in the relevant fields and presentations by public organizations involved with the dementias, a consensus panel consisting of representatives from neurology, psychiatry, geriatric medicine, epidemiology, psychology, family practice, neuropathology, nursing, and the public considered the evidence and formulated a consensus

The National Institutes of Health urges that this consensus statement be posted, duplicated, and distributed to interested staff.

statement responding to these questions:

1. What is dementia?
2. What are the dementing diseases, and which of them can be readily arrested or reversed?
3. What should be included in the initial evaluation of dementia?
4. What diagnostic tests should be performed, and when are these tests indicated?
5. What are the priorities for future research on diagnosing the dementias?

1.

What is Dementia?

Dementia is a clinical state with many different causes, characterized by a decline from a previously attained intellectual level. It is more or less sustained in time, arbitrarily measurable in months or years rather than in days or weeks. Although long lasting, some varieties of dementia may be arrested or reversed. The term "dementia" is not applied to isolated focal loss of function such as occurs in amnesia, aphasia, agnosia, or apraxia. The decline usually involves memory, other cognitive capacities, and adaptive behavior. There is usually no major alteration of consciousness. The patient may or may not be aware of the dementia. In almost all cases, there is significant deterioration of memory and of one or more other intellectual functions such as language, spatial or temporal orientation, judgment, and abstract thought. Some criteria for dementia require defects in one or more components of intellectual function other than memory; some require that the defect be global, that is, involve all components of intellectual function.

Dementia is a consequence of dysfunction of the brain, particularly of those parts of the cerebrum known collectively as the association areas, which integrate perception, thought, and purposeful action so that the person can adjust to and survive in the environment.

The onset of dementia is usually but not always insidious. The patient or family observes minor forgetfulness, restlessness or apathy, an increasing tendency to misplace things, small inconsistencies in some of the ordinary tasks of daily living, and repetitiousness of word or action. If the dementing process worsens, more disorganization of cognitive function takes place. Patients may fail at work, become lost in their own neighborhoods, fail to recognize people familiar to them, or reverse their sleep cycles. There may be hallucinations, delusions, or overt paranoid behavior. Some patients retain the shadows of their personalities even into severe dementia; others behave inappropriately and even antisocially. Depending on the pathological state that causes dementia, there may or may not be indications of brain disease beyond the cognitive and behavioral change. In some demented patients, changes in motor, sensory, and visual systems appear; concomitant disorders of extrapyramidal function are especially common.

Dementia is a very variable state. A patient may or may not be aware of his dementia. It may be progressive, as in the degenerative diseases, or static, as in a postbrain injury state. Even when progressive, the duration of decline may be slow or rapid, ranging from a few months to many years. The manifestations vary from disease to disease and from patient to patient within a given disease. There may be more than one underlying cause in the same patient. Patients may or may not have evidence of neuronal dysfunction other than that producing the dementia.

Dementia is distinguished from mental retardation, but a person who is mentally retarded can become demented when he declines from a previously attained level, as happens so often in Down's syndrome. Dementia is not psychosis: a patient with dementia may or may not be psychotic; a patient with psychosis may or may not be demented.

Many different disease states are capable of producing dementia. In this sense, we refer to *dementing diseases*. These diseases are divisible into two groups. In one group, the process inevitably produces dementia if it progresses through its full course; these are the conditions thought to affect the brain primarily or exclusively, such as Alzheimer's disease, Huntington's disease, and Parkinson-dementia complex. Other diseases may or may not produce dementia, depending upon whether or how the brain is affected. Examples are liver disease with portacaval encephalopathy, metabolic disorders such as hypothyroidism, or infectious disorders such as syphilis or acquired immune deficiency syndrome.

2.

What are the dementing diseases, and which of these can be readily arrested or reversed?

Dementia, a clinical syndrome, can be produced by numerous pathological states that affect the brain. These pathological states can be divided into those that appear, on the basis of our present knowledge, to be primary in the brain, such as Alzheimer's disease or Pick's disease, and those which are outside the brain and affect it secondarily, such

as the encephalitides or exogenous intoxications. A clinically useful division of dementia-producing pathological states is made into those that are progressive or fixed, such as Alzheimer's disease and hypoxic-ischemic encephalopathy of cardiac arrest, and those that are arrestable or reversible, such as chronic subdural hematoma or myxedema.

Some pathological states, if allowed to run their course, result inevitably in dementia; others may never go on to dementia or may produce only fragments of the dementia syndrome. Frequently, more than one pathological cause is operating to produce the dementia in an individual patient. The commonest example of this is the person with a progressive degenerative dementia who is taking an excess of a psychoactive medication that is having a potentiating effect upon the primary process.

The investigation of the patient is determined by these nosological considerations. The physician initially seeks out those causes of dementia that can be arrested or reversed. They may be found in all the classical categories of disease: intoxicant, infectious, metabolic, nutritional, vascular, neoplastic, genetic, and traumatic.

Arrestable or Reversible Causes of Dementia

Intoxications

Intoxications may result from medication or from nonmedication chemicals deliberately or accidentally ingested. Medications capable of producing dementia include the increasingly large number of neuroactive and psychoactive agents, the opiate analgesics, and the adrenocortical steroids. These are the obvious ones; however, even less obvious, frequently used medications may cause or aggravate dementia: anticholinergic preparations such as are used in movement disorders, allergic reactions, or gastrointestinal disorders; drugs used for cardiovascular purposes, such as antihypertensives; and even digitalis and its derivatives. Finally, multiple drugs in combination may have more than an additive effect.

Virtually all of the chemicals used in substance abuse from heroin to glue are capable of producing dementia. Other exogenous chemicals include carbon monoxide, carbon disulfide, lead, mercury, and manganese.

Any of these intoxicants, of whatever sort, may have lethal or irreversible consequences, but they are high on the list of the common causes of arrestable or reversible diseases that affect the central nervous system.

Infections

Any infection capable of involving the brain is capable of producing a dementing illness. Many cases of dementia are prevented from happening in the first place by the effective treatment of leptomeningitis and encephalitis, whether caused by bacteria, fungi, protozoa, or viruses. Chronic infectious processes, such as can be caused by bacteria (Whipple's disease), protozoa (syphilis), or fungi (cryptococcus), affect the brain in such a way that the process is reversible and arrestable, at least to a degree. Certain chronic viral illnesses, such as human immunodeficiency virus, are known to produce dementia with great frequency, but it is not known whether the agents that retard the process of AIDS will arrest or reverse the changes in the nervous system that lead to dementia. The agents responsible for conditions like Creutzfeldt-Jakob disease and progressive multifocal leukoencephalopathy are so far resistant to any kind of treatment.

Postinfectious encephalomyelitis, such as follows the viral exanthems, infrequently may produce enough damage to leave the patient demented.

Metabolic Disorders

Chronic diseases, tumorous or nontumorous, of thyroid, parathyroid, adrenals, and pituitary are subject to easy identification and generally are reversible. Pulmonary disease produces a dementia consequent upon hypoxia or hypercarbia. The encephalopathies of renal failure and hepatic failure respond up to a point to measures directed at underlying causes. The diabetic becomes vulnerable to a multitude of metabolic mechanisms related to the disease or to the treatment. It must be remembered that dehydration is the commonest metabolic abnormality of the older person with or without dementia.

A number of hereditary metabolic diseases often associated with dementia make their appearance for the first time in adult life. Examples are Wilson's disease (hepatolenticular degeneration), metachromatic leukodystrophy, the adrenoleukodystrophies, and the neuronal storage diseases.

Nutritional Disorders

Thiamine deficiency produces Wernicke-Korsakoff's encephalopathy, out of which may emerge Korsakoff's dementia. The dementia of Korsakoff's, once established, may undergo a degree of remission, but the pathological changes are irreversible. Thiamine deficiency is a preventable nutritional deficiency seen in the context of alcoholism, pernicious vomiting of pregnancy,

depression, or any other condition in which this deficiency occurs. There are different mechanisms by which pernicious anemia can produce dementia; not all of them are reversible. Folate deficiency is potentially reversible if recognized early. Pellagra, uncommon in developed countries but still a major problem in some parts of the world, shows a dramatic response to niacin even when the mental changes have been present for a long time.

Vascular

Management of the underlying states can arrest and sometimes reverse the dementias of cardiovascular origin. Hypertension, especially severe hypertension, is one of the most frequent causes of dementia. By producing cerebral infarctions, large and small, it is the commonest cause of multi-infarct dementia. Other causes are atherosclerosis and arteriosclerosis without hypertension, vasculitis, and emboli from the heart or elsewhere in the vascular system. Cardiac disease also produces dementia by single or repeated episodes of cerebral ischemia and hypoxia due to acute or intermittent disorders of cardiac function.

Chronic occlusion of extracranial arteries leading to the brain does not result in dementia in the absence of infarctions.

Space-Occupying Lesions

Chronic subdural hematoma may produce a dementia by itself, or it may complicate and add to the effects of other causes. It is not uncommon in dementias of older people, where the mode of presentation is often different from that seen in younger people.

Benign tumors of the brain produce dementia depending on their size and location. Notable are those on the orbital surface of the frontal lobe or on the medial surface of the temporal lobe because they may not be associated with other more familiar signs of cerebral tumor. Obstructive hydrocephalus may produce dementia in such benign lesions as cerebellopontine angle neurofibromas.

Malignant tumors of the brain frequently produce dementia. Only rarely is the dementia relieved by palliative treatment.

Normal Pressure Hydrocephalus

Normal pressure hydrocephalus produces a dementia associated with gait disturbance and urinary and fecal incontinence. It is a rare but frequently discussed condition. Some patients respond dramatically to shunting of the ventriculosubarachnoid reservoir.

Affective Disorders

Depression may be so severe that it produces a true cognitive deficit that is reversible with successful treatment. Depression commonly is present with other causes of dementia, especially Alzheimer's disease.

The Progressive Degenerative Diseases

The most frequent of the dementing diseases are not arrestable or reversible. They are, as far as it is known, primary in the brain and are divisible into two groups, those with no important neurological findings other than dementia and those with other prominent neurological signs.

Alzheimer's disease is the classical example of the first category. It is the most common of all the dementing diseases, increasing in frequency in the older age groups. Although not diagnosable in life with total certainty, a high probability in diagnosis can be attained by using the criteria established by the NINCDS-ADRDA Work Group of 1984. Pick's disease is the other condition in this category, but it is far less frequent than Alzheimer's.

The second category includes a multitude of diseases of the nervous system in which dementia may or may not occur. They include diseases of the basal ganglia (Parkinsons's, Huntington's), of the cerebellum (cerebellar and spinocerebellar degenerations, olivopontocerebellar degeneration), and of the motor neurone (amyotrophic lateral sclerosis). Some have more complicated anatomical distributions: Parkinson's-amyotrophic lateral sclerosis-dementia complex of Guam, progressive supranuclear palsy, progressive subcortical gliosis, and multiple system atrophy. It must be recognized that this is only a partial listing of these diseases. Taken all together, they do not compare with the very great frequency of Alzheimer's disease.

3.

What should be included in the initial evaluation of Dementia?

The history is the most important component of the initial evaluation; it should be obtained from both the family and the patient. Family members most responsible for and most often in contact with the patient should be consulted first, followed by other family members, friends, and neighbors. Community health workers, especially nurses and social workers, can provide important and objective information. Wherever possible, previous medical records should be reviewed.

A chronological account of the patient's current problems should

emphasize the mode of onset, duration of disease, and specific cognitive, memory, and behavioral changes, including such problems as becoming disoriented or lost in a familiar place, having difficulties with driving, or becoming repetitious, irritable, or agitated. Symptoms suggesting cerebral disease should be investigated. The medical history should include inquiries about relevant systemic diseases, trauma, surgery, psychiatric disorders, nutrition, alcohol and substance use, exposure to environmental toxins, and the use of medication, both prescribed and nonprescribed. The Hachinski scale is useful in organizing the patient's history relevant to cerebral vascular disease.

Family history should include questions about relatives who suffer from dementia, Down's syndrome, or psychiatric disorders.

The significance of a patient's behavioral changes needs to be considered within the social context, including cultural, ethnic, racial, educational, occupational, marital, and family background. Additionally, a physician should inquire about changes in the functional abilities, including dressing, grooming, toileting, eating, housekeeping, shopping, preparing meals, and managing finances.

The aim of the physical examination should be to detect not only the primary cause or causes of dementia but also coexisting abnormalities that may exacerbate the patient's disability. The neurological examination should be geared to the detection of focal lesions and signs of general brain dysfunction. In assessing mental status, it is desirable to include a published mental status test with known psychometric characteristics that can provide a baseline for subsequent evaluations. Physicians should consider administering the test themselves because it offers the opportunity to observe the patient's response to questions. At the same time, they can observe and inquire about the patient's mood and the presence of any hearing or visual impairment that may affect the validity of the testing of the mental state.

Examples of published mental status tests are the Mini-Mental State, the Blessed Information-Memory-Concentration test, and the Short Portable Mental Status Questionnaire. These are brief tests, requiring only 5 to 15 minutes for administration. They carry a relatively high risk of both false positives and missed cases. No single test, of any kind, will by itself establish a definitive determination of the presence of dementia; brief tests will provide rough documentation of the patient's mental state.

Short screening batteries, which require 10 to 30 minutes to give in clinical settings, are more satisfactory in the sense that they produce fewer false positive results and miss fewer cases. Examples of such short batteries are the Washington University SDAT Screening Battery and the Iowa Screening Battery for Mental Decline.

A patient should not be considered demented solely on the basis of a poor score on a mental status test or short battery. Identification of dementia in an elderly individual must take into account the cognitive changes that normally occur with aging; what is required for identification are changes that are greater than expected for the individual. Age-associated memory impairment (previously called "benign senescent forgetfulness") is a controversial condition that may be merely a manifestation of normal age-related changes in memory. Mild changes in memory are thought to be normal at age 50 in some people. Slight changes in spatial perception and attention are similarly regarded as normal at age 60. Small changes in abstract thinking and language are considered normal at age 70. A score suggestive of dementia should be considered clinically significant only if it is corroborated by other components of the initial evaluation, such as a strong evidence of deterioration by history or a clinical observation of deterioration on repeated visits. The clinician must be aware that premorbid mental dullness can produce a picture that may mimic early dementia. If there is an unresolved question of lifelong mental retardation, the patient should be referred to a psychologist who is experienced in testing such individuals.

The clinical diagnosis of dementia and the pathological state that causes it should not be considered a one-time or final process. Continuing observation over time is necessary to establish diagnosis for some patients and to identify complicating or superimposed conditions for others. Especially in patients with irreversible dementing diseases, continuing care requires repeated evaluations.

4.

What diagnostic tests should be performed, and when are these tests indicated?

The best diagnostic test is a careful history and physical and mental status examination by a physician with a knowledge of and interest in dementia and the dementing diseases. Such an evaluation is time consuming, but nothing else can replace it. Subspecialty consultation proves helpful in selected cases.

The laboratory tests that are used should be individualized based on the history and physical and mental status examination. Overtesting may expose the patient to discomfort, inconvenience, excess costs, and the likelihood of false positive tests that may lead to additional unnecessary testing. Undertesting also has hazards, for example, in elderly persons, where medical diseases may have nonspecific presentations such as dementia.

All patients with new onset of dementia should have several basic and standard diagnostic studies, with modifications to be made according to individual circumstances:

1. Complete blood count.
2. Electrolyte panel.
3. Screening metabolic panel.
4. Thyroid function tests.
5. Vitamin B_{12} and folate levels.
6. Tests for syphilis and, depending on history, for human immunodeficiency antibodies.
7. Urinalysis.
8. Electrocardiogram.
9. Chest x-ray.

Most of the readily reversible metabolic, endocrine, deficiency, and infectious states, whether causative or complicating, will be revealed by these simple investigations when combined with history and physical examination.

Other ancillary studies are appropriate in certain common situations:

1. Computed tomography of the brain (without contrast) is appropriate in the presence of history suggestive of a mass, or focal neurologic signs, or in dementia of brief duration. Unless such diagnosis is obvious on first contact, computed tomography should be done.
2. All medications that are not absolutely necessary should be discontinued.
3. Electroencephalograms are appropriate for patients with altered consciousness or suspected seizures, depending on the clinical circumstances.
4. Formal pyschiatric assessment is desirable when depression is suspected.
5. Inpatient hospitalization should be considered when the history is unclear, if the patient is suicidal, when an acute deterioration has occurred without apparent cause, or if the social situation precludes adequate observation.
6. Neuropsychological evaluation is appropriate (a) to obtain baseline information against which to measure change in cases in which diagnosis is in doubt, (b) before and following treatment, (c) in cases of exceptionally bright individuals suspected of early dementia, (d) in cases of ambiguous imaging findings that require elucidation, (e) to help distinguish dementia from depression and delirium, and (f) to provide additional information about the extent and nature of impairment following focal or multifocal brain injury.
7. Speech and language analysis can be very helpful. In some patients, complex language disorders can simulate dementia; in others, the skillful speech pathologist can help the patient and family to communicate better.

The role of other studies is controversial, and firm rules for their routine use are not appropriate. Undue weight should not be placed on isolated laboratory findings unless they are consistent with previous clinical information. Examples of these other studies include the following:

1. Magnetic resonance imaging is more sensitive than computed tomography for detection of small infarcts, mass lesions, atrophy of the brainstem, and other subcortical structures; it also may clarify ambiguous computed tomography findings. Inexperienced interpreters may make too much of ambiguous or nonspecific findings on magnetic resonance imaging.
2. Regional cerebral blood flow and metabolism measurements (positron emission tomography and single photon emission computed tomography) are research techniques that have no proven *routine* clinical value at the present time. Their value in predicting Huntington's and Alzheimer's disease in individuals at risk is under investigation.
3. Lumbar puncture is not routinely required in the initial evaluation of dementia. It should be performed when other clinical findings suggest an active infection or vasculitis. At present, cerebrospinal fluid markers for Alzheimer's disease are not sufficiently well developed to justify routine lumber puncture.
4. Electrophysiological techniques such as event-related potentials that are recorded using special electroencephalographic

techniques are not recommended for routine use.

5. Brain biopsy for nontumorous and noninfectious diseases rarely is justified except in a small number of unusual clinical situations.

6. Biological markers for progressive degenerative dementing diseases are still in the investigative stage. Although some give promise, they are not ready for widespread or routine use.

7. Significant major findings have been made on the molecular genetics of conditions like Huntington's and Alzheimer's diseases, but these findings have restricted usefulness at present.

8. Carotid ultrasound is of no value except sometimes in the search for the cause of infarcts.

5.

What are the priorities for future research on diagnosing the dementias?

Diagnosis of the dementing diseases has improved over the past 10 years. Nevertheless, there is room for improvement in accuracy of diagnosis. Advances in genetics and molecular biology have opened the door to new areas of research but are not immediately applicable to clinical diagnosis. While awaiting the development of definitive in vivo diagnostic tests, it is necessary to rely on autopsy correlation and validation. These remain essential for studies concerned with the search for diagnostic markers, neuropsychological findings, neuroimaging results, outcome of clinical therapeutic trials, and delineation of clinical-pathologic syndromes. Although it is impossible to list all the approaches to future research that may prove fruitful, the panel recommends that highest priority should go to research on the following:

1. Exploration of potential biological diagnostic markers, innovative as well as logical extensions of ongoing research, with special emphasis on families with autopsy-diagnosed dementias.

2. Evaluation of neuroimaging by long-term followup of patients, correlation with clinical and neuropsychologic findings, and tissue histopathology. Families with autopsy-diagnosed dementias should be given special attention.

3. Evaluation of results obtained with current neuropsychologic instruments in populations that differ in age, education, ethnic composition, and social or cultural background, using long-term followup and correlation with clinical, neuroimaging, and neuropathologic findings.

4. Assessment of the role of vascular disease in dementia by combining clinical, neuropsychologic, neuroimaging, and neuropathologic findings as well as by examining vascular risk factors.

5. Investigation of neuropsychologic test profiles characteristic of specific dementias and validation by means of clinical, neuroimaging, and neuropathologic findings.

6. Design of multivariate studies to determine the optimal combination of diagnostic strategies, including elements of the history and physical examination, mental status, and specialized tests needed to differentiate the dementias common in each age group.

7. Investigation of the mechanisms by which various drugs, nonpsychoactive as well as psychoactive, induce or precipitate a dementia syndrome.

8. Exploration of the mechanisms by which depression induces or precipitates a dementia syndrome.

9. Investigation of the less common degenerative diseases, such as Pick's disease, progressive supranuclear palsy, olivopontocerebellar degeneration, and progressive subcortical gliosis.

Conclusion

Dementia is a clinical state, diagnosable only by clinical methods. Every patient with dementia deserves precise assessment, not only of the fact of dementia, but of the manifestations and the manner in which the disability is produced. Dementia can be caused by a multitude of different dementing diseases, some of which are arrestable or reversible, and many of which are preventable.

The first approach to a patient with suspected dementia is a careful clinical evaluation. A laboratory test, whether chemical, biological, imaging, or psychological, should never be used as a substitute for the physician's time, expertise, and clinical judgment. Because dementia is primarily a behavioral diagnosis, the initial medical evaluation should include an assessment of how well the patient functions in his or her daily life as well as a family history and neurological and standardized mental status examinations. Relatives, friends, and neighbors often can provide information especially valuable in assessing a patient suspected of having dementia.

The diagnosis of dementia has become more accurate over the past 10 years, but thorough assessment still cannot be done rapidly. Because serious implications are inherent in making a diagnosis of irreversible dementia and in missing any conditions that may be arrested or reversed, physicians are urged to take the time necessary to make this thorough evaluation and to refer patients to specialists when they want further confirmation of clinical findings.

Because large gaps still exist in current knowledge on the diagnosis of dementia, the panel has made specific recommendations for further research that will result in improving the differential diagnosis of dementing diseases.

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* U. S. GOVERNMENT PRINTING OFFICE: 1987-181-295:51128

Special Communication

Reprinted from the Journal of the American Medical Association
July 18, 1980, Volume 244
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Senility Reconsidered

Treatment Possibilities for Mental Impairment in the Elderly

Task Force Sponsored by the National Institute on Aging

• The brain is particularly vulnerable to insults occurring anywhere in the body. In some older persons, the brain may respond to insult by slowly developing impairment of intellectual functions (dementia) or abruptly showing significant changes in mental state (delirium). Sometimes the two coincide, producing a variable clinical picture with features of both dementia and delirium. It is crucial for health professionals, public planners, and lay persons to recognize that many curable physical and psychological diseases in the elderly produce intellectual impairment that may be hard to distinguish from irreversible brain disease.

(*JAMA* 244:259-263, 1980)

IT IS generally accepted that there are changes in some intellectual functions in the elderly just as there is some loss in physical abilities with aging. Normal aging, however, does not include gross intellectual impairment, confusion, depression, hallucinations, or delusions. Such symptoms are due to disease and indicate the need for diagnosis and treatment.

Estimates are that approximately 10% of persons older than 65 years have clinically important intellectual impairment.[1-4] In a survey of nursing homes published in 1978, respondents to a questionnaire reported that 50% to 75% of the residents in their facilities were intellectually impaired.[5]

Intellectual impairment in the elderly may be due to conditions that can be cured, to conditions that with our current state of knowledge show an inexorable downhill course, or to conditions that can be ameliorated with treatment. Although there are no definitive studies identifying the frequency of reversible intellectual impairment in the elderly, data from small samples suggest that 10% to 20% of all persons older than 65 years having such impairment have reversible conditions.[6,7]

Symptoms

Mental impairment in the elderly can be either global or limited to specific functions. Global disturbances include dementia and delirium, in which many facets of intellectual function are impaired. Korsakoff's syndrome and aphasias secondary to localized cerebral lesions are examples of disturbances of single functions.

"Dementia" refers to global impairment of intellectual functions. In a normally conscious and responsive patient, dementia is a powerful clue in differential diagnosis. As consciousness becomes abnormal, dementia becomes less useful in diagnosis, although the absence of dementia may be diagnostically important. Dementia cannot be demonstrated in stuporous patients. The onset of dementia may be sudden, as in severe anoxia of relatively short duration, but in most cases, dementia develops slowly and insidiously. Nonprogressive dementia can occur, for example, after anoxia, but most often dementia either is steadily progressive or progresses in discrete steps. Although the definition of dementia specifies that the intellectual impairment is global, the deterioration may be patchy rather than uniform. Moreover, while dementia is frequently irreversible, it may be reversible or partially reversible. The dementia that may accompany hypothyroidism, for example, is usually reversible.

Early symptoms of dementia noted by relatives, employers, or friends, and frequently by patients themselves, are failing attention, memory, and declining mathematical ability. Errors of judgment, irritability, personality changes, loss of sense of humor, or poor orientation may indicate to those around the patient that intellectual function is progressively deteriorating. This impression can be

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confirmed and documented by mental status examination. One can quickly test for orientation for time, place, and person; short-term memory; arithmetic calculation; ability to name objects; comprehension of spoken and written language; ability to write a spontaneous sentence; and ability to copy simple geometric figures.[8-14] The information obtained is usually enough to confirm the presence of dementia in an alert, demented patient.

"Delirium" refers to an abnormal mental state that usually includes mild to severe global intellectual impairment and a number of other manifestations of disordered mental function. Fluctuating alertness, tremors, restlessness, confusion, stupor, diminished attention span, and decrease in amount of sleep with day-night sleep reversal, as well as hallucinations (particularly visual), delusions, autonomic or other reactions such as rapid pulse, flushed skin and dilated pupils, and intense emotional states are all common. The onset of delirium is usually abrupt and obvious but may be insidious and easily overlooked. The course of delirium is often relatively short and may be terminated by death, recovery, or progression into another symptom complex.

In the elderly, delirium is frequently superimposed on recognized or unrecognized preexisting dementia. When dementia is the substrate for delirium, much of the turmoil of delirium may be muted or absent. Patients who are thus doubly afflicted seem to experience either the abrupt onset of a new dementia or the worsening of an established one. In either case, the superimposed delirious state may be overlooked and its cause left untreated.

Causes

The reversible causes of impaired intellectual function are listed in the Table. Although not every case of these disorders can be cured, many can, and others can be substantially alleviated. The most common causes of reversible impaired intellectual function are therapeutic drug intoxication, depression, and metabolic or infectious disorders.

Either dementia or delirium may be caused by the adverse effects of medication. An enormous number of drugs have been implicated, including diuretics, digitalis, oral antidiabetic drugs, analgesics, anti-inflammatory agents, sedatives, and psychopharmacologic agents.

The incidence of depression increases greatly with advancing age. Although the common manifestations of depression in the elderly frequently do not differ substantially from those of depression in younger persons, elderly patients may deny depressed mood more often and have instead multiple somatic complaints, hypochondriasis, or pain. An extremely important feature of depression in the elderly is that it may be accompanied by a mild-to-profound reversible dementia. Severe cases of such dementia may make it extremely difficult to distinguish depression from Alzheimer's disease, and misdiagnosis is not uncommon in settings where extensive multidisciplinary assessment is not available.

The aged brain is extremely sensitive to the internal environment. Almost any disorder that alters this environment—cardiac, pulmonary, renal, or hepatic failure; endocrine disorders; water and electrolyte disturbances; anoxia; anemia; infections; nutritional deficiencies; and hypothermia or hyperthermia, for example—may produce dementia or delirium. Intracranial lesions, eg, hemorrhagic, neoplastic, or infectious, can also cause intellectual deterioration, as can sensory deprivation and intoxication with various therapeutic and nontherapeutic chemical substances.

There are relatively few disorders which cause irreversible dementia but two of them (Alzheimer's disease and multi-infarct dementia) account for approximately 80% of the dementias of old age. Most of the irreversible diseases tend to produce dementia rather than delirium. Some exceptions are head injury with brain trauma, major stroke, and anoxic brain damage; even these often progress to dementia.

The most common cause of severe intellectual impairment in the elderly is senile dementia of the Alzheimer's type, a disease characterized clinically by relentlessly progressive dementia, alertness in the early stages of the disease, and a course leading to death in five to ten years. Dementia dominates the presentation, but depression, hallucinations, delusions, and neurological manifestations may occur. At autopsy there are cerebral atrophy and characteristic histological changes consisting of neurofibrillary tangles in the neurons and degenerative neuritic plaques. A similar or identical disease occurs in middle-aged persons. The term "Alzheimer's disease" will be used in this article, regardless of the age of onset of the disease. A much rarer type of degenerative disease called Pick's disease is difficult to distinguish from Alzheimer's disease.

Dementia from multi-infarct disease is less common than Alzheimer's disease, but nonetheless, it is responsible for most of the remaining cases of intellectual impairment in the elderly. Multi-infarct disease is due to multiple occlusions of small cerebral arteries with widely distributed areas of infarction. Hypertension or diabetes is often present, and the early clinical picture may be characterized by signs of arterial disease elsewhere in the body. The dementia progresses slowly, in a stepwise rather than a steady fashion, is usually patchy rather than uniform, and finally becomes dominant. With the onset of dementia, multi-infarct disease is called multi-infarct dementia. Focal neurological abnormalities are often present in multi-infarct dementia, as are dysarthria and an abnormal gait with short steps. The limbs in multi-infarct dementia are spastic with brisk reflexes.

Other causes of irreversible dementia in old age include Huntington's disease, which is transmitted genetically as an autosomal dominant trait, usually appears in middle age, and is characterized by dementia and choreiform movements. The course is progressive and commonly leads to death within 15 years of the first manifestations. Creutzfeldt-Jakob disease, a rare disorder caused by a filtrable agent transmissible to chimpanzees and other animals, is characterized by a rapidly progressive dementia and devastating neurological abnormalities. Death often occurs within a year.

Diagnosis

Examination of a mentally impaired elderly patient should include

a detailed history, comprehensive physical examination, mental status and psychiatric evaluation, and appropriate ancillary examinations. Psychological consultation and examination may be helpful. Because of the wide range of the differential diagnosis, a detailed history may be exceptionally important. It should be obtained from the patient (insofar as possible), from the best-informed relative or acquaintance available (since the nature of the disease may make the patient's account unreliable), and from past medical records. A past history of depression or a reversible illness similar to the presenting syndrome may be of great help. A careful social history of events that might have affected the patient's emotional status is important in the diagnosis of the disease. An inventory should be made of prescription and over-the-counter drugs that the patient is taking. This involves more than simply talking to the patient. An inspection of the patient's medicine cabinet or other storage place may disclose that the patient is still taking drugs prescribed long ago or may have similar prescriptions from several physicians.

The physical examination should be thorough since disease in almost any organ system may cause dementia or delirium. The neurological examination is particularly important. The detection of flapping tremor (asterixis) is especially valuable because it is frequently present in cases of mental impairment associated with metabolic derangements but absent in Alzheimer's disease, multi-infarct dementia, and depression. The mental status examination may disclose or confirm the presence of intellectual impairment. A single examination provides quantification of intellectual impairment, and serial examinations permit the physician to follow the extent and tempo of decline or improvement. Several simple mental status tests are described in the current literature.[8-14] If it has not been done earlier, care should be taken at this stage of evaluation to determine if the patient is aphasic, because the inability to communicate may be mistaken for dementia. In addition to the mental status examination, an effort should be made to elicit the common symptoms of depression described above. Finally, paranoid symptoms

Reversible Causes of Mental Impairment

	Dementia	Delirium	Either or Both
Therapeutic drug intoxication			Yes
Depression	Yes		
Metabolic			
a. Azotemia or renal failure (dehydration, diuretics, obstruction, hypokalemia)			Yes
b. Hyponatremia (diuretics, excess antidiuretic hormone, salt wasting, intravenous fluids)			Yes
c. Hypernatremia (dehydration, intravenous saline)		Yes	
d. Volume depletion (diuretics, bleeding, inadequate fluids)			Yes
e. Acid-base disturbance		Yes	
f. Hypoglycemia (insulin, oral hypoglycemics, starvation)			Yes
g. Hyperglycemia (diabetic ketoacidosis, or hyperosmolar coma)		Yes	
h. Hepatic failure			Yes
i. Hypothyroidism			Yes
j. Hyperthyroidism (especially apathetic)			Yes
k. Hypercalcemia			Yes
l. Cushing's syndrome	Yes		
m. Hypopituitarism			Yes
Infection, fever, or both			
a. Viral			Yes
b. Bacterial			
Pneumonia		Yes	
Pyelonephritis		Yes	
Cholecystitis		Yes	
Diverticulitis		Yes	
Tuberculosis			Yes
Endocarditis			Yes
Cardiovascular			
a. Acute myocardial infarct		Yes	
b. Congestive heart failure			Yes
c. Arrhythmia			Yes
d. Vascular occlusion			Yes
e. Pulmonary embolus		Yes	
Brain disorders			
a. Vascular insufficiency			
Transient ischemia		Yes	
Stroke			Yes
b. Trauma			
Subdural hematoma			Yes
Concussion/contusion		Yes	
Intracerebral hemorrhage		Yes	
Epidural hematoma		Yes	
c. Infection			
Acute meningitis (pyogenic, viral)		Yes	
Chronic meningitis (tuberculous, fungal)			Yes
Neurosyphilis			Yes
Subdural empyema			Yes
Brain abscess			Yes
d. Tumors			
Metastatic to brain			Yes
Primary in brain			Yes
e. Normal pressure hydrocephalus	Yes		
Pain			
a. Fecal impaction			Yes
b. Urinary retention		Yes	
c. Fracture		Yes	
d. Surgical abdomen		Yes	
Sensory deprivation states such as blindness or deafness			Yes
Hospitalization			
a. Anesthesia or surgery			Yes
b. Environmental change and isolation			Yes
Alcohol toxic reactions			
a. Lifelong alcoholism	Yes		
b. Alcoholism new in old age			Yes
c. Decreased tolerance with age producing increasing intoxication			Yes

Reversible Causes of Mental Impairment (cont)			
	Dementia	Delirium	Either or Both
Alcohol toxic reactions (cont)			
d. Acute hallucinosis		Yes	
e. Delirium tremens		Yes	
Anemia			Yes
Tumor—systemic effects of nonmetastatic malignant neoplasm			Yes
Chronic lung disease with hypoxia or hypercapnia			Yes
Deficiencies of nutrients such as vitamin B_{12}, folic acid, or niacin	Yes		
Accidental hypothermia		Yes	
Chemical intoxications			
a. Heavy metals such as arsenic, lead, or mercury			Yes
b. Consciousness-altering agents			Yes
c. Carbon monoxide			Yes

often accompany dementia but may exist as part of paranoid disorders without dementia. An effort must therefore be made to distinguish between the two.

Ancillary examinations should include the following: (1) hematologic examination (blood cell counts, hematocrit reading, hemoglobin level, and sedimentation rate); (2) urinalysis (albumin, glucose, and ketone levels and microscopic examination); (3) stool examination, including a test for occult blood; (4) evaluations of levels of serum urea or BUN and glucose; serum electrolytes (sodium, potassium, carbon dioxide content, chloride, calcium, phosphorus); bilirubin; B_{12}; and folic acid; (5) tests for thyroid function; (6) serological test for syphilis; (7) chest roentgenogram; (8) ECG; and (9) computerized tomography (CT scan) of the brain.

The relative ease of administering most of the tests required for the differential diagnosis and the gravity of dementia and delirium favor their early use, but the number and order of tests conducted will depend on the particular presentation of the case, the judgment of the physician, and the ease with which the diagnosis can be made.

Computerized tomography has proved to be an immensely valuable diagnostic procedure. Its worth is such that many physicians believe it should be used early in the investigation of every case of undiagnosed mental impairment in the elderly. Some physicians prefer to employ it after simpler tests have been given a chance to establish the diagnosis. The CT scan can be instrumental and sometimes crucial in the diagnosis of subdural and epidural hematoma, tumor, intracranial hemorrhage, abscess, subdural empyema, hydrocephalus, and cerebral infarction. It can also identify cerebral atrophy. However, a radiological diagnosis of cerebral atrophy in the elderly may reflect only aging of the brain and not superimposed disease. A reversible dementia may well be present even though cerebral atrophy is diagnosed by CT scan. The CT scan is therefore useful in establishing a diagnosis of focal intracranial disease but not in making a definitive diagnosis of Alzheimer's disease. Other radiological examinations, such as arteriography or radionuclide scanning, may be indicated by the clinical findings.

The clinical findings may suggest that an examination of CSF be made. The diagnostic value of this procedure should be weighed against its dangers, particularly if hemorrhage into the CNS or increased intracranial pressure is thought to be present. With rare exceptions, a CT scan should be done before a lumbar puncture is performed. The scan may demonstrate a lesion such as a hemorrhage or other mass, with the result that CSF examination becomes unnecessary. The chief value of CSF examination for the patient with dementia or delirium is the discovery of CNS infection. The risks may be reduced by using a fine needle and removing only a small quantity of fluid.

In some cases more detailed psychological examination than that of a simple mental status test may be useful.[15] Information regarding the qualitative aspects of a patient's performance on such tests as the Wechsler Adult Intelligence Scale, the Bender-Gestalt Visual-Motor Test, or the Wechsler Memory Scale may be useful in distinguishing depressive pseudodementia from other forms of cognitive impairment. A comprehensive neuropsychological test battery is also available.[16]

Treatment

If there is a definitive diagnosis of a reversible disease, the physician will be familiar with its treatment or have ready access to the appropriate information. If dementia is present, no definitive diagnosis is possible, and if the patient is not obviously in good spirits, then a therapeutic trial with an antidepressant drug in the context of psychotherapeutic counseling should be seriously considered.

Even if an elderly patient has an irreversible disorder, frequently much can be done to reduce the severity of its manifestations through symptomatic and supportive therapy. An intellectually impaired elderly person is not likely to remain oriented for time, place, and person unless someone repeatedly supplies information on those items. Persons who work with the intellectually impaired elderly should be aware of this need.

Treatment of hypertension may be appropriate for patients with multi-infarct dementia. Extreme care must be exercised in reducing blood pressure, however, because of the danger of further decreasing cerebral blood flow and because of the cerebral effects of many antihypertensive agents.

Intellectually impaired elderly patients should be moved to new locations as infrequently as possible, because it is difficult for marginally oriented persons to cope with unfamiliar surroundings. Suitably structured environments can use a patient's residual strengths—color coding to identify locations in nursing homes is an example of a useful technique.

Certain aspects of the care of the elderly are important in both treatment and prevention and apply to the healthy elderly as well as the mentally impaired. Sensory deprivation, both visual and auditory, is common and may lead to disorientation. The mental disturbance that may occur when both eyes are covered after cataract surgery is a dramatic example of an effect of sensory depriva-

tion. Lighting should be bright, and appropriate eyeglasses should be provided. Looking directly at a partially deaf person and speaking clearly and slowly in a moderately loud voice is often helpful. In some instances, hearing aids may improve hearing. The importance of hearing is emphasized by the occurrence of interpersonal difficulties and even paranoia in the deaf elderly.

Routine hygiene and the careful treatment of even minor illnesses are important in maintaining the mental integrity of the elderly. The elderly tend to have numerous simultaneous disorders that interact detrimentally. Regardless of their primary problems, old persons are vulnerable to complications, including falls, nighttime confusion, bedsores, incontinence, and fecal impaction. These and major illnesses presenting without their classic manifestations may aggravate or cause dementia or delirium.

The extreme sensitivity of the aged brain to a wide variety of medications is a source of trouble. The elderly are more susceptible than younger persons to the side effects of many drugs, and ordinary doses may lead to adverse reactions. Necessary medications should be introduced gradually when possible. At the onset of any mental impairment, all medications should be reviewed. Care must be taken in discontinuing drug therapy, however; at times a patient may have to be hospitalized for this purpose.

The elderly person's social and environmental situation should be given appropriate consideration. A key feature in maintaining mental health in old age seems to be continued mental as well as physical activity.

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Printed and Published in the United States of America

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---updated November 1988

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NIA GRANTEES MAY HAVE UNCOVERED KEY TO BRAIN PATHOLOGY IN ALZHEIMER'S DISEASE

Two eminent neuroscientists have combined their research interests and uncovered a critical piece of information on why brain cells die in Alzheimer's disease.

Dr. Carl W. Cotman at the University of California at Irvine and Dr. Dennis J. Selkoe at Harvard Medical School and Brigham and Women's Hospital in Boston, Massachusetts have found that a fragment of the protein in neuritic plaques may possess the ability to regulate growth of nerve cells in the healthy human brain.*

Neuritic plaques, which are dense, insoluble deposits of amyloid protein, are among the major pathological hallmarks of Alzheimer's disease. Until now, scientists have not known what role amyloid protein plays, if any, in healthy brain tissue or why an increasing number of large clusters of amyloid appear in the brains of Alzheimer patients.

Earlier NIA-supported studies revealed that the abnormal amyloid protein is made up of fragments of a larger protein that is normally spread across nerve cell membranes. Scientists also have discovered the approximate location of the gene for the fragment, called the amyloid precursor protein, and have identified the building block amino acids that constitute it.

In the current investigations, Drs. Cotman and Selkoe synthesized the first 28 amino acids of the amyloid protein and tested the effects of this synthetic peptide on nerve cells grown in tissue culture. Nerve cells grown in tissue culture do not

(MORE)

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*The results of this research, funded by the National Institute on Aging (NIA), appear in the March 17, 1989 issue of Science magazine, "Amyloid B Protein Enhances the Survival of Hippocampal Neurons in Vitro," by Janet S. Whitson, Dennis J. Selkoe, and Carl W. Cotman.

survive long, but in the presence of the synthetic peptide, the cells stayed alive for longer periods of time. These results demonstrated that amyloid has a trophic, or growth enhancing, effect on nerve cells.

On the basis of these experiments, Drs. Cotman and Selkoe speculate that plaque formation in Alzheimer's disease may signal the nerve cells' attempt to mount a defense against the degenerative process and to compensate for the damage that occurs as the disease progresses. The investigators also speculate that events in the early stages of Alzheimer's disease may lead to the production of an abnormal amyloid protein that malfunctions and contributes to the progress of the disease.

Scientists at the National Institute on Aging are hopeful about the results of this work, as well as recent research on nerve growth factor, one of several known trophic factors that enhances the survival of injured nerve cells. As investigators learn more about how and why cells die in Alzheimer's disease, it may become possible to slow the progression of the disease using nerve growth factor or similar substances.

Prior to this latest research, Dr. Selkoe was widely recognized for his research on amyloid protein as well as on the proteins that form the characteristic neurofibrillary tangles of Alzheimer's disease. Dr. Cotman distinguished himself with his pioneering studies of synaptic plasticity, the ability of damaged or diseased nerve cells to repair themselves. Both of the investigators have received long-term research support from the NIA and are recent recipients of NIA grants for Leadership and Excellence in Alzheimer's Disease (LEAD).

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NATIONAL INSTITUTE ON AGING

NEWS NOTES

FOR RELEASE
March 14, 1988

For more information contact:
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ALZHEIMER'S AND RELATED DEMENTIAS COST $88 BILLION, HEALTH ECONOMISTS SAY

An analysis of the cost of Alzheimer's disease and related dementias suggests that $88 billion was lost in 1985 due to these illnesses. The cost estimate is based on those patients who are 65 or older and suffer from Alzheimer's disease, multi-infarct dementia, or mixed cases of both. This group accounts for about 85 percent of all dementias in the population. Alzheimer's disease represents approximately 60 percent of the total costs of the dementias considered in this study.

The analysis was carried out by NIA health economist Dr. William Cartwright and colleagues Dr. Lien-Fu Huang at Howard University in Washington, D.C. and Dr. Teh-wei Hu at the University of California, Berkeley. According to the investigators, direct patient care costs, including nursing home care and social services, were $13.26 billion. This figure is conservative because it includes only the additional costs of care, or those above and beyond the average costs of medical care for other conditions not related to the dementing illness.

A recent study by the U.S. Office of Technology Assessment, Losing a Million Minds, reports that the government pays only 10 to 15 percent of costs for Alzheimer's disease, mostly for direct medical care, imposing a heavy burden on the affected families. According to Dr. Cartwright and his colleagues, dementia patients, unlike victims of other major killers, typically spend a number of years receiving care at home until the disease progresses to a point where institutionalization becomes necessary. Most of the in-home care required by Alzheimer's patients is for custodial (nonmedical) care--supervision and assistance with daily tasks such as eating, bathing, and dressing--and is not normally covered by government entitlement programs. The indirect cost of such home care, $31.46 billion (provided mainly by family members), is much higher than that for direct care. Another $43.17 billion of economic loss is due to loss of productivity during the extended period of illness and to premature death.

(More)

The investigators note that the total amount is conservative for a number of reasons, one being that it does not take into account the stress-related costs to caregivers and their families. Another reason that the figures are probably low, the investigators explain, is because they included in their analysis total costs for only the 3.5 percent of nursing home patients admitted for dementia. For most of the 50 percent, or over 600,000, of nursing home residents thought to suffer from dementia, just the additional cost of care was counted.

This information on the costs of dementia is essential for the development of new social, health, and economic policies for affected patients and their families, to determine research priorities, and for supporting aging and medical research.

Results of the analysis are published in the January-February issue of Public Health Reports.

# # # # # # #

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Q alzheimer's disease &A:

NIH Publication No. 85-1646
Reprinted May 1985

U.S. DEPARTMENT OF HEALTH
AND HUMAN SERVICES
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National Institutes of Health

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What is Alzheimer's disease?

A: Alzheimer's disease (pronounced altz'hi-merz) is a little-known but surprisingly common disorder that affects the cells of the brain. It is a disease that produces *intellectual impairment* in some 2.5 million American adults. While experts formerly believed that Alzheimer's disease occurred most often in persons under age 65, this disorder is now recognized as the most common cause of severe intellectual impairment in older individuals.

The changes most commonly associated with Alzheimer's disease occur in the *proteins* of the *nerve cells* in the cerebral cortex—the outer layer of the brain—leading to an accumulation of abnormal fibers. Under the ordinary microscope these changes appear as a tangle of *filaments*. These *neurofibrillary tangles* were first described in 1906 by *Alois Alzheimer*, a German neurologist.

New and highly sophisticated instruments and techniques—such as the *electron microscope* which can magnify cells more than a hundred thousand times—have revealed other changes in the brain that are characteristic of the disease. Scattered throughout the cortex, groups of *nerve endings* degenerate and disrupt the passage of *electrochemical signals* between the cells. These areas of degeneration have a special appearance under the microscope and are called *plaques*. The larger the number of plaques and tangles, the greater the disturbance in intellectual function and memory.

What are its symptoms?

A: At first, the individual experiences only minor and almost imperceptible symptoms that are often attributed to emotional upsets or other physical illnesses. Gradually, however, the person becomes more forgetful, particularly about recent events. The individual may neglect to turn off the oven, may misplace things, may recheck to see if a task was done, may take longer to complete a chore that was previously routine, or may repeat already answered questions. As the disease progresses, memory loss increases and other changes, such as confusion, irritability, restlessness, and agitation, are likely to appear in personality, mood, and behavior. Judgment, concentration, orientation, and speech may also be affected. In the most severe cases, the disease may eventually render its victims totally incapable of caring for themselves.

There are many different patterns in the type, severity, and sequence of changes in *mental* and *neurological functioning* that result from Alzheimer's disease. The symptoms are progressive, but there is great variation in the rate of change from person to person. In a few cases, there may be a rapid decline, but more commonly, there may be many months with little change. Limitations in physical activity during the later stages may cause the person to have less resistance to pneumonia and other physical illnesses that may shorten remaining life expectancy by as much as one-half.

Although the person with

PARKINSON'S DISEASE—a neurological disorder characterized by rhythmical muscular tremors, rigidity of movement, stooped posture, short accelerating steps in walking, and masklike expression.

PERNICIOUS ANEMIA—a blood disorder characterized by a deficiency in red cells thought to result from the failure of the stomach lining to secrete an adequate amount of the factor needed to absorb vitamin B–12; occurs most commonly in later life and may affect the nervous sytem.

PLAQUES—a localized abnormal area found in the brain of a person with Alzheimer's disease.

PROTEIN—a chemical compound consisting of a long chain of amino acids that contain a special grouping of nitrogen and hydrogen; produced by living cells or obtained as essential components of the diet.

TOXICOLOGY—a science that deals with the action, detection, and treatment of poisonous substances.

VASCULAR DISORDER—abnormal functioning resulting from changes in the blood vessels.

VIROLOGY—a science that deals with viruses and viral diseases.

HYDROCEPHALUS—a condition characterized by the excessive accumulation of fluid in the cavities of the brain, causing a thinning of the brain; may be present at birth or occur later in life.

IMMUNOLOGY—a science that deals with the processes through which individuals are able to resist, or become sensitive to, a particular disease.

INTELLECTUAL IMPAIRMENT—a diminished capacity to think or understand.

L-DOPA—a chemical similar to one which naturally occurs in the brain and is used as a medicine in the treatment of Parkinson's disease.

MENTAL FUNCTIONING—the normal actions of the mind.

METABOLIC DISORDER—a disturbance in the physical and chemical processes by which chemical compounds in the body are produced, maintained, and transformed into energy.

NERVE CELL—a neuron, the basic unit of the nervous sytem consisting of a cell body and its threadlike extensions for receiving and transmitting impulses.

NERVE ENDING—the fine branchlike terminations of the extensions that carry impulses away from or toward the body of a nerve cell.

NEUROFIBRILLARY TANGLE—an accumulation of abnormal fibers in the nerve cells in the cerebral cortex.

NEUROLOGICAL FUNCTIONING—the normal activities of the nervous sytem.

Alzheimer's disease may deny or be unaware of the full extent of his or her limitations—especially later in the course of the illness—the inexplicable changes in essential functions are a source of deep frustration for those afflicted and for their loved ones.

How is the diagnosis made?

A: Before a diagnosis of Alzheimer's disease is made, other illnesses which may cause memory loss must be excluded. The condition must be differentiated from the mild and occasional forgetfulness that sometimes occurs during normal aging. Depression, which is fairly common in elderly individuals facing a variety of stressful situations, may also affect memory.

Approximately one-half of elderly men and women with severe intellectual impairment are victims of Alzheimer's disease. About another fourth of the overall group suffer from *vascular disorders*, especially multiple strokes, and the balance have a variety of other conditions; for example, brain tumors, abnormal thyroid function, infections, *pernicious anemia*, adverse drug reactions, and abnormalities in the spinal fluid system (*hydrocephalus*). The specific diagnosis is very important as some causes of mental decline, other than Alzheimer's disease, can be readily treated.

Each person suspected of having Alzheimer's disease should have thorough

physical, neurological, and psychiatric evaluations. *Computerized tomography (CT scan), electroencephalography,* and occasionally special studies of the spinal fluid system are often required for accurate diagnosis. Comprehensive blood studies, including tests for detecting several *metabolic disorders*, must also be carried out as part of the evaluation.

After other diseases have been ruled out, a firm diagnosis of Alzheimer's disease can usually be made on the basis of medical history, mental status, and the course of the illness. The electroencephalogram may show a general slowing of the brain waves and may help confirm the presence of Alzheimer's disease. Periodic neurological examinations and psychological testing are useful in evaluating the progress of the disease.

What causes Alzheimer's disease?

A: Alzheimer's disease is a neurological illness. But why plaques and neurofibrillary tangles develop in the cortex of the brain has not been determined.

It seems clear that Alzheimer's disease is not caused by hardening of the arteries. There is no evidence that it is contagious. Although emotional upsets and stress may temporarily affect the person's mood and behavior, they do not cause the disease.

Alzheimer's disease occurs in 2 to 3 percent of the general population. The

GLOSSARY

ALZHEIMER, ALOIS—(1864–1915) a German physician who studied the relationship of changes in the structure of the nervous system to disease, and who first described the changes in the disease that carries his name.

BIOCHEMISTRY—the science that deals with the chemistry of living things.

BRAIN ENZYME—a protein that accelerates a specific chemical reaction in the brain.

CHOLINE ACETYLTRANSFERASE—an enzyme that stimulates the production of acetylcholine, a chemical compound active in the transmission of nerve impulses.

COMPUTERIZED TOMOGRAPHY (CT OR CAT SCAN)—a new diagnostic technique using a computer and X-rays to obtain a highly detailed image of the section of the body being studied.

ELECTROCHEMICAL SIGNAL—the transmission of a nerve impulse by electrical and chemical changes.

ELECTROENCEPHALOGRAPHY (EEG)—the recording of the electric activities of the brain by means of wires placed painlessly on the scalp; useful in detecting tumors, epilepsy, and brain damage.

ELECTRON MICROSCOPE—one in which an electron beam, instead of light, produces a greatly magnified image.

FILAMENT—a delicate fiber or thread of protein found in the brain cells.

HISTOLOGY—the branch of anatomy that deals with the minute structure of cells, tissues, and organs in relation to their function.

but new studies have demonstrated a higher prevalence of the disease. Theories are now being formed about its cause—theories that may ultimately contribute to the knowledge needed to halt or even reverse the illness. For example, scientists have recently identified a striking reduction—as much as 90 percent—in a particular *brain enzyme (choline acetyltransferase)* that is involved in the passage of nerve signals. If a deficient chemical process rather than the destruction of cells themselves proves to be involved, then health professionals may ultimately employ restoratives to lessen the symptoms of Alzheimer's disease in much the same way as *Parkinson's disease* is treated with *L-dopa*.

Alzheimer's disease is a very specific and major disease whose cause must be determined before it can be treated and prevented. Recent dramatic advances in medical instrumentation and technology have generated further interest in the diagnosis, treatment, and prevention of Alzheimer's disease. To stimulate new research on Alzheimer's disease, the National Institute on Aging, the National Institute of Neurological and Communicative Disorders and Stroke, and the National Institute of Mental Health have co-sponsored a series of workshop-conferences. In response to this expanding interest, studies are now underway or in the planning stages on a large variety of possible risk factors and on biological abnormalities in the brains of those with Alzheimer's disease. There is still much misinformation and lack of understanding about Alzheimer's disease, however. You can help by learning more about it and sharing the knowledge with others.

additional increase in its occurrence within the same family, up to 4 to 8 percent, may represent a slight hereditary disposition or an undetermined environmental factor.

Several scientists are applying the newest knowledge and research techniques in *histology, virology, immunology, toxicology*, and *biochemistry* to the study of human brain tissue removed at autopsy. Although there are now a number of promising clues, the determination of the actual cause of Alzheimer's disease requires further scientific investigation.

What is the treatment for Alzheimer's disease?

A: As yet, physicians do not know how to prevent or how to cure Alzheimer's disease. However, proper medical care can reduce many of its symptoms and sound guidance can assist the person and family in coping with its significant impact on their lives.

It is imperative that the person be under the care of a physician. The physician may be a neurologist, a psychiatrist, or a family physician or internist who can consult with a neurologist. Most important, the physician selected must be willing to devote the time and interest required to closely monitor treatment, and to answer the many questions that are bound to arise during the variable course of the illness in any one individual. A physician will also be needed to treat any other

physical ailments that may further complicate the course of the disease.

Drugs are not the only answer, but judicious use of tranquilizers can lessen agitation, anxiety, and unpredictable behavior. Appropriate medication can also improve sleeping patterns and can be used to treat the depression which often accompanies the illness. Proper nourishment and fluid intake are very important, particularly in the aged, but special diets or supplements are usually not necessary. Carefully guided exercise is of value, and physical therapy can help if difficulties arise in physical functioning.

Activities should be maintained at as close to a normal level as possible. A person should try to continue his or her daily routine, physical activities, and social contacts, and should be encouraged and assisted, if need be, to do a little more than he or she feels can be done. It may be helpful to provide memory aids that assist the individual in day-to-day living: a prominent calendar; lists of daily tasks; written reminders about routine safety measures; and directions to, and labeling of, frequently used items.

Although, in general, it is best to maintain an ordered environment so that a person does not have to continuously learn new things, it is important not to restrict a person from trying something new. For example, an individual with Alzheimer's disease may do very well on a trip when accompanied by a supportive family member or friend.

During the early phases of Alzheimer's disease, the person can most often be cared for by the family at home. When the condition becomes more severe, however, a special setting with professional staff and full-time care may be required. If needed, such an arrangement can be in the best interests of both the individual and the family.

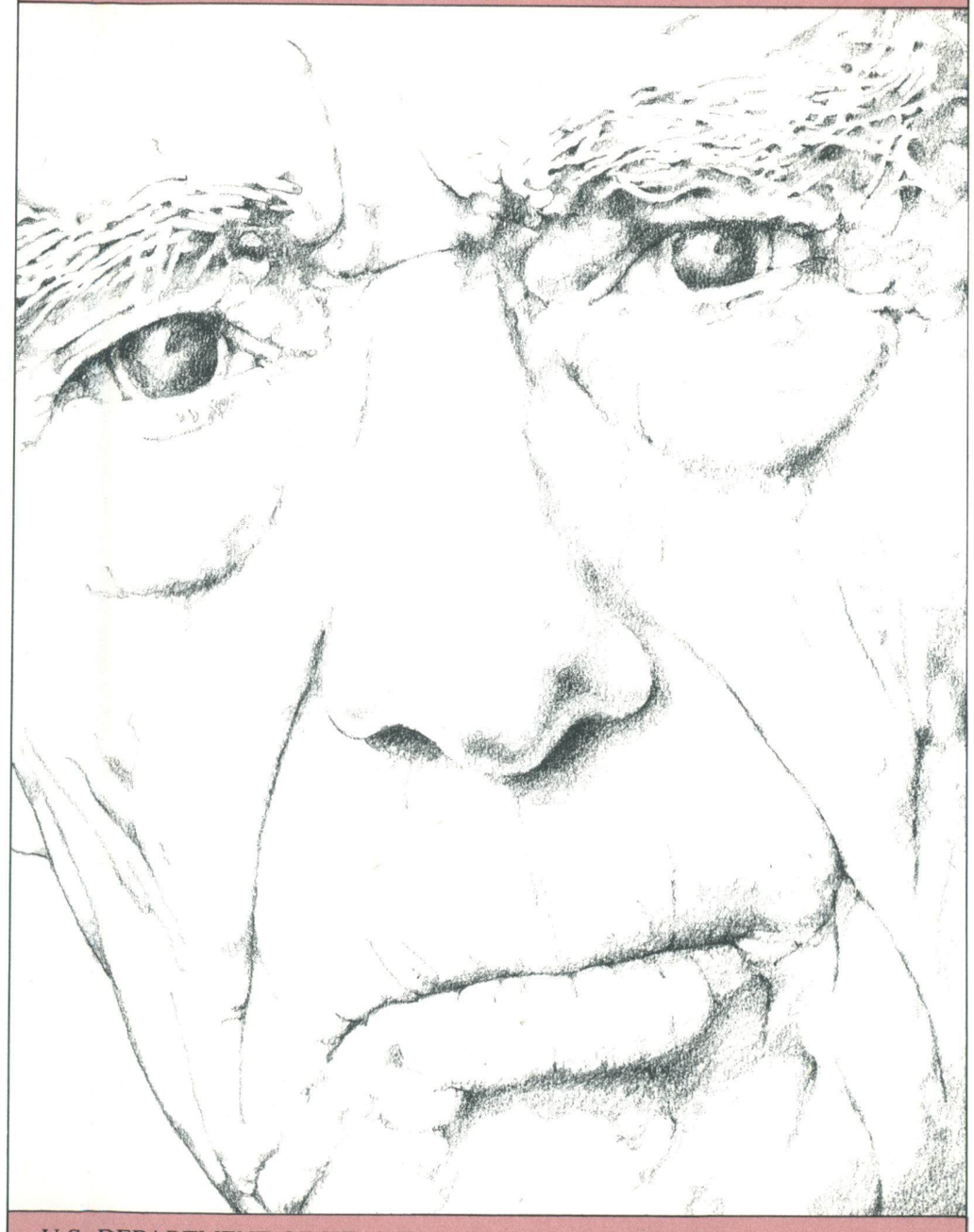
Understandably, the person afflicted with Alzheimer's disease finds it difficult to comprehend the changes taking place in thinking and behavior. Family and friends will want to know how they can help. There will be questions about the activities the person can engage in with safety, how much encouragement should be given to carry out a familiar activity that has become painfully frustrating, and how to explain the memory loss to neighbors. Such questions can only be answered individually, depending on the person and the particular phase of his or her illness. The physician or an associate—a psychologist, nurse or social worker—can be helpful in meeting this need. Family members may also benefit by sharing their experiences with other families who are facing the same problems through one of several supportive groups which are just now being established across the country.

What is being done to learn more about Alzheimer's disease?

A: Physicians' attitudes towards an illness are shaped by whether or not they believe the illness is widespread, and whether its course can be arrested or reversed. Until recently, Alzheimer's disease was believed to be a rare occurrence.

National Institute on Aging
NIH Publication No. 84-2500
July 1984

PROGRESS REPORT ON ALZHEIMER'S DISEASE: Volume II



U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
National Institutes of Health

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Executive Summary

Alzheimer's disease, the major form of old age "senility," is the cause of serious confusion and forgetfulness in some 2,000,000 elderly Americans and a probable contributor to the institutionalization of as many has half of the more than one million elderly in long-term care facilities.

Since 1976, when the interest of three Federal research organizations—the National Institute on Aging (NIA), the National Institute of Neurological and Communicative Disorders and Stroke (NINCDS), and the National Institute of Mental Health (NIMH)—focused on the prevalence and possible causes of this disorder, government research activities on the dementias of aging have increased by more than 800 percent.

A major inroad came when it was demonstrated that Alzheimer's disease is a brain disorder and not a normal consequence of aging. Since then, some studies have looked at the biological mechanisms of Alzheimer's disease, in particular the role and chemical composition of structures that irreversibly alter aging brain cells and play a major role in the disease.

Other scientists have employed a variety of methods to investigate what causes Alzheimer's disease. Research on certain well-established chemical changes in the Alzheimer brain have become more intriguing recently because of evidence of the selective destruction of cells in a part of the base of the brain which provides these chemicals to higher brain regions. Studies on the contribution of aluminum to the disease's development have been linked with a new environmental hypothesis. Scientists have furthered their understanding of the effects of viral infections on the central nervous system in diseases similar to Alzheimer's disease. Genetic studies have shown a clustering of Alzheimer cases in some families although no consistent pattern of genetic transmission has been demonstrated.

Research is just beginning to address whether psychosocial factors may contribute to the causes or development of Alzheimer's disease. To date, behavioral sciences research has focused mainly on the search for diagnostic tests, on changes in language use, and on special supports needed by families of victims.

On the basis of early findings of biomedical, social, and behavioral studies, a number of scientists are developing projects aimed at improving care and treatment for Alzheimer victims. Clinicians need a more sensitive and reliable diagnostic test or some kind of "marker" which will detect the disorder in its earliest stages. Other clinical researchers are attempting to compensate for established declines in brain chemistry as a way of treating the serious symptoms of Alzheimer's disease. This research is set in the context of major advances in the field of neuroscience, including advances, aided by computer technology, in the ability to view and understand the workings of the living human brain.

The following report provides a brief overview of the state of scientific study of Alzheimer's disease.

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NIMH	728	815	790	1315	2151	4700	4800	5000	5600
NINCDS	2314	2333	2422	2844	4960	5427	6243	8678	10924
NIAID	—	—	—	1381	1775	1394	1256	1041	1435
Total	3899	4648	5172	9682	13097	16717	20353	26567	36439

Conclusion

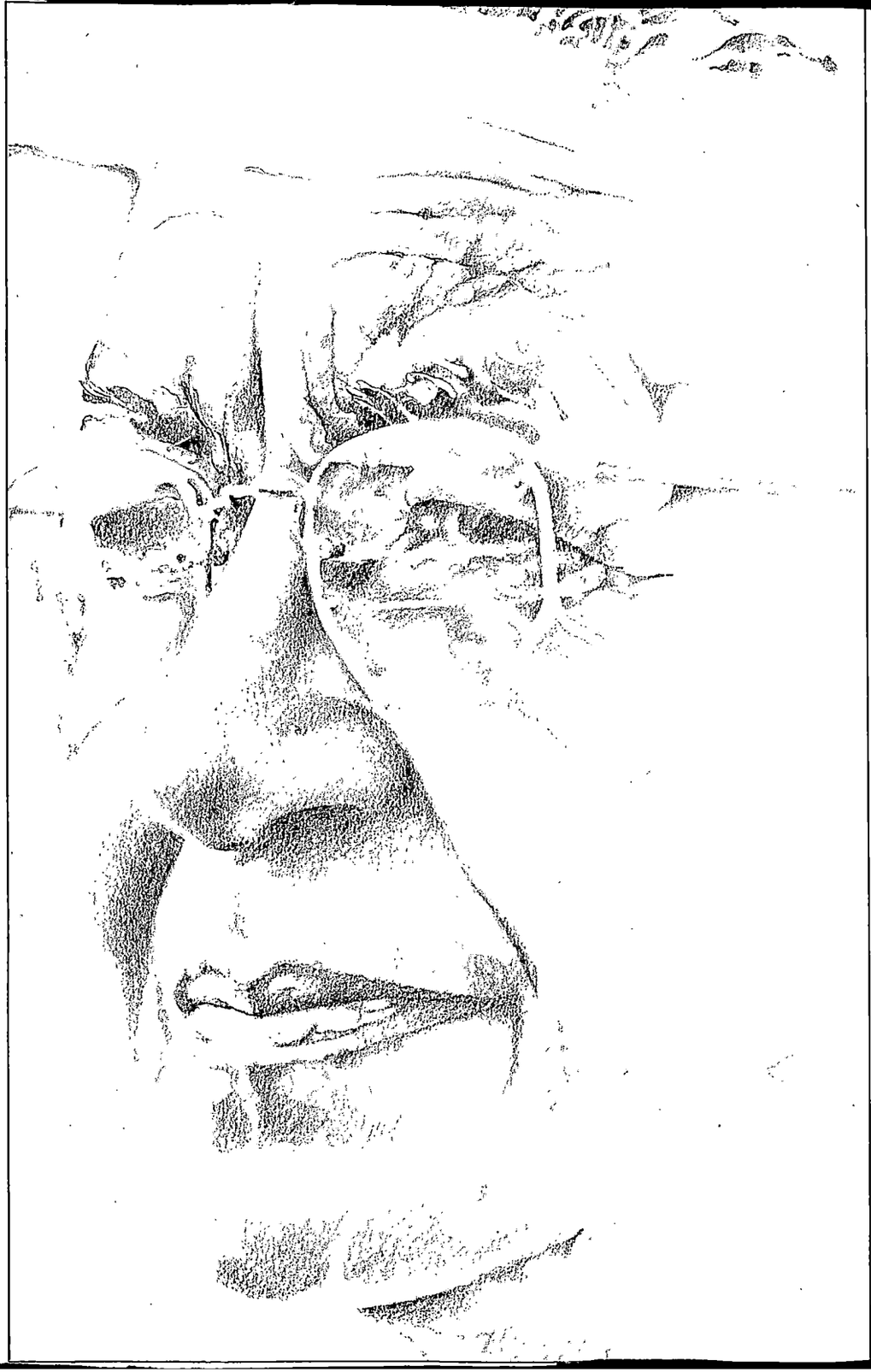
Over the past decade, research scientists have made major advances in their studies of aging and the brain. At the same time, scientists, health professionals, policymakers, and the public have experienced a growing awareness of the impact of Alzheimer's disease.

Since 1976, Alzheimer's disease has become a major priority for Federally-supported scientific research. Scientific studies of the diagnosis, causes, nature, incidence, prevalence, and course of Alzheimer's disease have established a solid foundation for research on the care, and possible treatment of its victims. At some future date, we may be able to cure or even prevent Alzheimer's disease. Much of this is due to the increased interest and growing cooperation among the Federal research agencies responsible for studies on aging, neurological disorders, and mental health.

Introduction

Alzheimer's disease is indeed a disease of catastrophic proportions. Now regarded as the major form of old age "senility," it is a surprisingly common disorder that affects the cells of the brain. While experts formerly believed that Alzheimer's disease only occurred in persons under 65, this disorder is now recognized as the most common cause of severe intellectual impairment in older individuals. Whether the classic form of Alzheimer's disease, which was first described in a middle-aged adult, is identical in cause, mechanisms, and course to Alzheimer's disease in old age is a matter of some controversy. In this publication, Alzheimer's disease refers to cases of early onset and to cases which occur after age 65.

The major debilitating symptoms of Alzheimer's disease include serious forgetfulness—particularly about recent events—and confusion. At first, the individual experiences only minor and almost imperceptible symptoms that are often attributed to emotional upsets or other physical illnesses. Gradually, however, the person becomes more forgetful and this may be reported by anxious relatives. The person may neglect to turn off the oven, may misplace things, may recheck to see if a task was done, may take longer to complete a chore that was previously routine, or may repeat already answered questions. As the disease progresses, memory loss and such changes in personality, mood, and behavior as confusion, irritability, restlessness, and agitation, are likely to appear. Judgment, concentration, orientation, writing, reading, speech, motor behavior, and naming of objects may also be affected. Even when a loving and caring family is available to give support, the victim of Alzheimer's disease is most likely to spend his or her last days in a nursing home or long-term care institution. At this time, there is no cure.



In one of several studies on senile dementia, NIMH scientists are continuing their investigations of neurofibrillary tangles in Alzheimer's disease. For some time, it has intrigued these investigators that nerve cells with neurofibrillary degeneration may be functionally impaired, but do not seem to rapidly deteriorate and die. If aluminum is, in fact, responsible for some of the degenerative brain changes in Alzheimer's disease, then attempts to remove this metal from the human body could have significant effects on the course of the illness. Following the lead of Czechoslovakian investigators who have suggested that aluminum interacts with fluoride ions and is in this way excreted from the body, scientists at the NIMH Adult Psychiatry Branch are now conducting a long-term study of the effects of sodium fluoride on the course and outcome of Alzheimer's disease. Results in the first patients studied are sufficiently encouraging to warrant continuation of this project. David Shore and Richard Wyatt expect to complete this pilot study during the fall of 1984.

Intramural Initiatives

The NIA Laboratory of Neurosciences (LNS) clinical program, established in 1980, is involved in an intensive investigation of brain metabolism in relation to normal human aging and dementia. In September 1982, Stanley I. Rapoport, LNS chief, and Neal R. Cutler, chief of the LNS clinical program, together with a staff of research neurologists, psychologists, and other health professionals admitted the program's first inpatients thus initiating a series of activities focusing primarily on the dementias and related neuropathological diseases of the elderly. Studies look closely at Alzheimer's disease and at multi-infarct dementia, which is caused by a series of minor strokes.

These studies of dementia are set in the context of a clinical program which examines the normal aging process from biochemical, cardiovascular, and general physiologic perspectives, including careful evaluation of brain function. The primary clinical goals of the program are 1) to develop a clear picture of brain physiology in normal aging and age-related disease; 2) to evaluate the changing pharmacokinetics and pharmacodynamics of various antihypertensives and central nervous system agents in the elderly; 3) to develop a better understanding of the causes, courses, and treatments of different forms of dementia; and 4) to encourage other NIH components to focus their clinical studies on the growing aging population.

Rapoport and his staff hope to use the results of their work to eventually design pharmacological approaches to treat reversible cognitive defects of aging and irreversible dementia and to understand better the neurochemical changes that occur in Alzheimer's disease.

The principal research efforts of Thomas N. Chase and the NINCDS intramural staff are directed towards the rational development of improved drug treatments for nervous system disease. Of particular interest are the investigators' attempts, using human subjects as well as animal models, to relate the activity of particular neurotransmitter systems such as the dopamine system, to specific brain functions. New drugs are then evaluated in animal models and in man for their ability to selectively modify these systems and thus ameliorate debilitating neurologic or psychiatric changes.

Biological Mechanisms

Glucose metabolism is one of three major interconnected measures of brain activity—the other two are brain blood flow and brain oxygen consumption. New noninvasive machinery which uses computer technology, allows simple tests of glucose metabolism and, in turn, provides a direct measure of activity in any given brain region. National Institutes of Health scientists and others using positron emission tomography (PET) and a compound similar in structure to glucose to measure glucose metabolism have come up with some fascinating findings about the workings of aged healthy and diseased brains.

Using PET to scan the normal aging brain, Stanley I. Rapoport, Ranjan Duara and their fellow scientists in the NIA Laboratory of Neurosciences have found no significant age-related alterations in brain glucose metabolism.[1] These investigators tested 40 men, aged 21 to 83, and found this was true for some several dozen regions of the brains that they scanned. These studies suggest that the healthy aged brain is as active and efficient as the healthy young brain. Of current interest to the investigators is why their findings are inconsistent with changes known to take place in the size and weight (i.e., the number of cells) of the brain as it ages, as well as findings of other investigators who have reported drops in glucose metabolism with age, and the controversial findings which suggest that brain blood flow and oxygen consumption may or may not change with age. Future studies by Rapoport and his colleagues will continue to build upon and analyze the results of this work. In the meantime, the investigators' findings are beginning to provide age-related normal values for glucose metabolism in the brains of healthy men of all ages.

PET scans are also beginning to show that various parts of the brain deteriorate at different rates as Alzheimer's disease progresses. NINCDS scientists Norman L. Foster, Thomas N. Chase and their associates have demonstrated that lowered metabolic rates in different parts of the brain can be linked to Alzheimer patients' inability to perform certain physical tasks.[2] The investigators selected 16 Alzheimer's patients who suffered from varying degrees of apraxia, a loss of voluntary movement without actual paralysis, and asked the patients to mimic, pantomime, or identify 75 body movements. Patients responded with varying success; different patients had different types of difficulties in performing tasks. On the basis of these and other preliminary test results, the investigators have suggested that Alzheimer patients with brain damage on the right side have difficulty mimicking or imitating actions, while those with damage on the left side are unable to follow verbal commands. According to Foster, other factors may affect how well a patient performs a task, including the complexity of the task and whether or not the action has a purpose. This may eventually help in clinical practice as physicians are better able to diagnose Alzheimer's disease and to treat patients.

Molecular Pathology

The changes most commonly associated with Alzheimer's disease occur in the proteins of the nerve cells of the cerebral cortex (outer layer of the brain) and lead to an accumulation of abnormal tangled fibers called neurofibrillary tangles. An important study of these characteristic nerve cell changes has revealed some unusual and unexpected findings. For several years, Dennis Selkoe, a neuropathologist and neurologist at the McLean Hospital in Belmont, Massachusetts, has received NIA grant support for his studies on the role and chemical composition of elements within normal and abnormal brain cells. Much of his work has focused on neurofilaments, elements within the cell that are made up of long hair-like strands of protein. In Alzheimer's disease, proteins like these bind together and twist into spiral-like configurations called paired helical filaments (PHF). Masses of PHFs form the characteristic neurofibrillary tangles of Alzheimer's disease. It is possible that these changes can be linked to cell death.

NIA-supported investigator Gary Gibson is building upon these earlier findings in an attempt to stimulate calcium concentrations and increase the synthesis and release of acetylcholine. Gibson and his colleagues have discovered a close link between the drop in synthesis and release of acetylcholine in healthy aged rats. These decreases are not as dramatic as those seen in Alzheimer's disease, and do not result in the general decrease in acetylcholine levels that is typical of Alzheimer's, but are nonetheless connected with certain learning and memory problems in animal studies. Since both synthesis and release of the neurotransmitter are dependent upon calcium concentrations, the investigators injected the rats with a drug which stimulated oxygen metabolism, increased calcium concentrations, and, in turn, improved old rats' performance on certain tests which involved learning.

While some investigators have attempted to increase acetylcholine synthesis indiscriminately in all cholinergic cells, and others are trying to prevent the otherwise fast breakdown of acetylcholine once it is synthesized, Gibson and his colleagues are trying to increase the ability of the cell to produce acetylcholine only when it is needed. These investigators have found a means to selectively pinpoint the sites at which the neurotransmitter is released and to program its release when the cell is active. Such an approach may ultimately benefit Alzheimer patients by allowing treatment with a minimum of side effects.

The first studies in this area involved ingestion of the drug choline chloride, which not only produced some rather unpleasant side effects, but failed to increase acetylcholine production in the brain. Other early studies employed pure forms of lecithin, the dietary source of choline with the same intent of increasing acetylcholine production. Lecithin increased the level of choline in the blood more than choline chloride, continued to have this effect for a longer period of time, and had no serious side effects—but also showed no consistent or marked benefit.

In 1978, research at the Bronx VA Hospital suggested that physostigmine, a drug which blocks the otherwise fast breakdown of acetylcholine in the brain, had a positive effect on the memory of elderly Alzheimer patients, but that the dose required to do so varied from subject to subject.[11] Use of the drug, however, was plagued by problems. It was not practical for Alzheimer patients since it had to be given by injection and its effects lasted less than one hour. Now, a research team supported by the NIA and the NINCDS at the Albert Einstein College of Medicine may have overcome some of the difficulties inherent in the use of this drug. Using an oral form of physostigmine, Leon Thal found marked improvement in six out of eight Alzheimer patients when the drug dose was carefully planned for each individual and given in combination with lecithin. The drug's effect lasted longer than the investigators anticipated so that memory improvement was still noticeable on the morning after the drug was administered. Also, side effects such as nausea and cramps were only apparent when the patient received more than the optimal dose to improve his/her memory. With support from the NIA, Thal hopes to expand these studies and to begin work on tetrahydroaminoacridine, a drug which also acts to slow breakdown of acetylcholine but may be safer and more effective than physostigmine.

At the Burke Rehabilitation Center in White Plains, New York, scientists are studying yet another approach to treatment of Alzheimer's disease. It is known that a variety of normal functions, critical to the life of brain cells, are controlled by calcium. Typically, calcium concentrations in the cell are maintained at a very low level, increasing only when the cell is stimulated and prepared to release neurotransmitters to other cells or other parts of the cell. At this point, it becomes crucial for calcium concentrations to increase temporarily.

Several studies of the aging brain have suggested that calcium activity decreases with aging, possibly compromising cell communications. This is an interesting finding when coupled with the knowledge that acetylcholine is one of several neurotransmitters partially influenced by calcium.

Selkoe and his colleagues have found that the proteins in Alzheimer tissue are highly resistant to standard protein solvents and that the molecules of the PHF's bind tightly together to form an extremely rigid "cross-linking" structure.[3] This is not the first time that cross-linking has been observed in aging human tissue. Other examples include the changes that take place in the formation of cataracts. In their most recent studies, Selkoe and his colleagues have compared the mechanisms responsible for cross-linkage in the lens of the aging eye to what may be going on in the aging brain. In the lens, a particular enzyme called transglutaminase appears responsible for the binding of protein. Selkoe has recently completed studies marking the presence of this enzyme in the human brain. Furthermore, the investigators have experimentally induced the development of a rigid molecular structure —although different in form from the PHF—by adding this enzyme to normal filaments. Future studies will expand the attempt to find out what causes the formation of structures that age and irreversibly alter brain cells, and play a major role in Alzheimer's disease.

With continued Federal support, Selkoe and his colleagues have developed what may become a definitive diagnostic test for Alzheimer's disease. In animal experiments, the investigators have developed an antibody which can selectively label the paired helical filaments which characterize Alzheimer's disease, and clearly distinguish these structures from normal brain proteins. Before Selkoe's pioneering work, studies had consistently suggested that virtually all proteins in Alzheimer tissue were similar to proteins in healthy aged brain tissue.

Because this new procedure entails surgical removal of a small section of the brain, the investigators caution that the current value of their work is somewhat limited. For the present time, their findings provide a powerful tool for studying the basic changes that take place in the brain as Alzheimer's disease progresses. Their findings might also help quickly identify Alzheimer's disease at autopsy. Before this work can proceed in living individuals, however, careful and sensitive attention must be given to the benefits and risks of brain biopsy in diagnosis.



Clinical Research

A number of scientists, including clinicians, gerontologists, biochemists, neuropathologists, neurophysiologists, psychologists, mathematicians, and many others, are employing the early findings of biomedical, social, and psychological studies to design clinical research projects—in particular, studies aimed at improving diagnosis, some of which were highlighted above, and studies aimed at improving treatment.

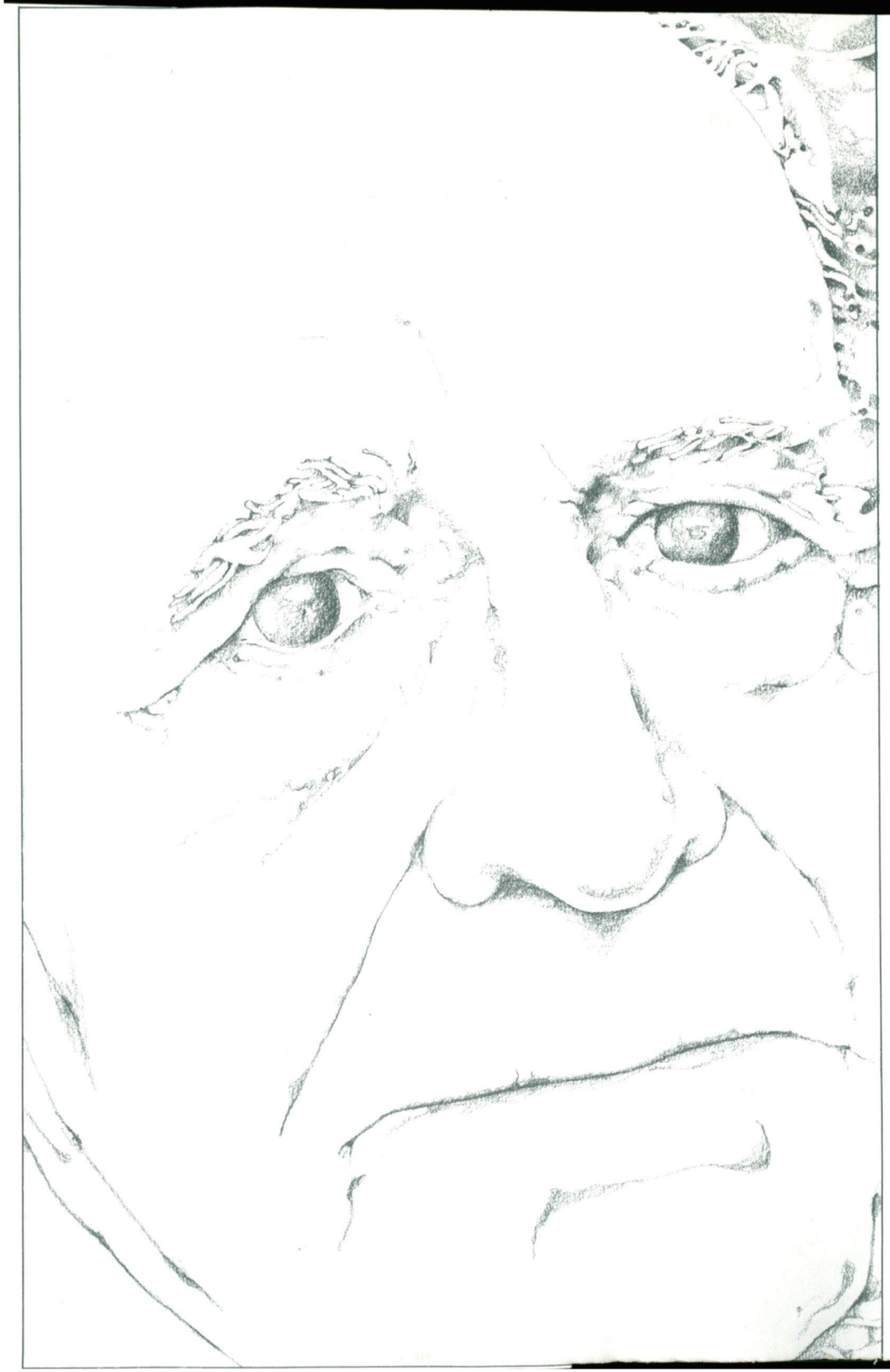
Sleep Studies

At the University of Washington, investigators receiving support from the NIMH, NIA, and the Veterans Administration are attempting to determine if the sleep and wake patterns of older individuals can be used to detect the presence and monitor the progress of Alzheimer's disease. In a series of sleep laboratory experiments, Patricia Prinz and her colleagues have looked at healthy young and old subjects and at patients with a diagnosis of Alzheimer's disease. Her findings in older healthy adults confirm early work on "normal" sleep patterns in the elderly: older people experience less of certain "stages" of sleep and awaken more frequently throughout the night than healthy young adults. She also found, however, that these and other changes were significantly more pronounced in Alzheimer patients, including frequent awakenings. The more advanced the disease, the more severe the changes.[10]

In her more recent studies, Prinz finds that impaired sleep is evident even in the very early stages of Alzheimer's disease and that the changes which occur are striking enough to differentiate healthy subjects from patients with severe, moderate, or even mild cases of the disease. In the next part of her investigation, Prinz will examine the sleep/wake patterns of elderly individuals who have complaints of memory loss to see if she has indeed found a "marker" to detect early cases of Alzheimer's disease.

Treatment Approaches

As noted above, one of the most consistent changes in Alzheimer's disease involves a decrease in the activity of the chemicals collectively comprising the brain's cholinergic system. While recognizing that Alzheimer's disease probably involves more than one neurotransmitter, basic scientists have attempted to determine what causes this particular decline and clinical scientists have attempted to compensate for this deficit as a way of treating the serious symptoms of Alzheimer's disease.



The Search For a Cause

In a decade marked by major advances in the fields of neuroscience and aging research, scientists have employed a variety of methods to investigate the possible cause(s) of Alzheimer's disease. Studies have looked at the roles of deleterious changes in brain chemistry, trace metals, and slow-acting viruses, as well as the roles of heredity and of changes in the aging immune system.

Biochemical Studies

Since the first reports in the mid 1970's, research scientists have been studying evidence of a significant and progressive decrease in the activity of the enzyme choline acetyltransferase (ChAT) in the brain tissue of Alzheimer patients. ChAT is a crucial ingredient in the chemical process which produces acetylcholine, a neurotransmitter involved in both learning and memory. Until recently, the most exciting findings were those which showed a link between this change in neurochemical activity and changes in both cognition (such as memory loss and disorientation) and the physical appearance of Alzheimer brains, particularly the number of characteristic plaques (degenerated nerve cell pieces which form around a fibrous core in the cerebral cortex). In order to explore further the relationship between ChAT and Alzheimer's disease, scientists are using new techniques such as monoclonal antibodies to help map areas of the brain where ChAT is present. Other current studies are aimed at expanding our understanding of a host of chemicals in human aging and dementia.

Recent studies at the Johns Hopkins University bring us closer to understanding what causes this decline in the brain's complex chemical activity. In studying the brains of Alzheimer victims, NINCDS/NIA/NIMH grantees Donald Price and Joseph Coyle find a marked loss of nerve cells in a part of the base of the brain called the nucleus basalis.[4] Some patients with classical Alzheimer's disease have been shown to lose as many as 90 percent of these cells. Scientists are intrigued by the possibility of a link between this loss and the decrease in cholinergic activity: the nucleus basalis produces acetylcholine and utilizes the neurotransmitter and its enzymes in communicating with the brain's cortex via connecting pathways. It has been known for some time that aging produces a loss of cells in the brain's cortex. But NINCDS-supported investigations involving meticulous counting of nerve cells indicate that there is no major loss of cells in the brain's outer layer. Therefore, normal cell loss has never been able to explain the severe degree of cholinergic deficiency—between 75 and 95 percent—in this part of the Alzheimer brain. Since the loss of acetylcholine is so detrimental in Alzheimer patients, and the nucleus basalis now

appears to be one of the major sources of the substance, researchers hope to learn why nerve cells of the nucleus basalis seem to be selectively destroyed in Alzheimer's disease. Scientists are also interested in these findings because they indicate that brain centers innervating higher brain centers may be important in the development of Alzheimer's disease.

Trace Metal Studies

A new and controversial finding reported by scientists at the University of Vermont and the National Institute of Neurological and Communicative Disorders and Stroke has linked the results of two separate avenues of research on Alzheimer's disease—research that suggests that aluminum may contribute to the disease's development, and research that probes the excess incidence of dementia in three separate populations.

With grant support from the NIA, Daniel Perl of the University of Vermont has extended his earlier findings of accumulations of aluminum within the affected nerve cells of subjects showing the classic neurofibrillary tangles of Alzheimer's disease. In a collaborative study, Perl and NINCDS intramural scientists Gajdusek, Garruto, Yanagihara, and Gibbs reported high accumulations of aluminum, iron, and calcium in the brains of Chamorro natives of Guam who had died of amyotrophic lateral sclerosis (ALS) or parkinsonism-dementia.[5] This population is adversely affected by these two chronic disorders, both of which were previously suspected to be transmitted by a slow-acting virus. For several years, Gajdusek and his colleagues at the NINCDS have been studying the possible implications of Guam's environmental deficiency in calcium and magnesium and excess of aluminum and other metals.

Researchers in the field of aging have kept a watchful eye on studies in Guam because of the similarities between the parkinsonism-dementia syndrome and Alzheimer's disease. In both disorders, there is an excessive accumulation of neurofibrillary tangles in the brains of victims that is associated with severe dementia and death.

These latest findings by Perl, Gajdusek and colleagues reconfirm Perl's earlier work linking high concentrations of aluminum in the brain to the development of neurofibrillary tangles, as well as work of Japanese investigators in both Guam and Japan. NINCDS scientists are exploring the possibility that secondary hyperparathyroidism caused by lack of calcium and magnesium in the environment provokes an accumulation of metal ions within brain tissue.

There is a serious need for further research on the experiences and needs of families of Alzheimer patients. As the primary source of care for those who suffer from dementia, the family bears most of the economic and emotional burden of the disease which might otherwise fall on social institutions. Moreover, research is needed on the possible contributions of family reactions to the course of the disease in the patient.



With support from NIMH, Steven Zarit of the University of Southern California will build upon earlier research on strategies for coping. Zarit and his colleagues have found that health professionals can greatly reduce the amount of stress that impedes a caregiver's ability to function by 1) providing information about the disease, 2) offering alternative solutions for day-to-day problems, and 3) providing an atmosphere whereby relatives, friends, or other caregivers can offer much-needed support.[9] According to the investigators, it is important —but rarely the case—that health professionals take the time to answer the many questions relatives will ask about the causes of the illness, medical treatments that may or may not be helpful or harmful, and what the illness will do to the patient's behavior. Such information is critical to developing reasonable solutions to practical problems the patient may have with eating, sleeping, and other routine behaviors. It is also important to offer caregivers individual or family counseling or to provide a structured environment in which they can discuss their experiences and solutions with others in the same situations. In the end, say the investigators, it is the ability of the caregiver to develop and/or maintain good coping skills, and to be able to count on support from family and friends, which will determine his or her ability to continue providing care, regardless of the severity of the dementia.

At the University of Michigan, Dorothy Coons and her colleagues have obtained private funding from the American Association of Retired Persons to quantify further the experiences of families. The investigators developed and distributed a questionnaire to 510 families of Alzheimer victims. Of the 75 percent who returned completed questionnaires, most were caring for relatives at home. Of those who had placed a relative in a long-term care institution, most had maintained the patient at home for as long as possible.

In what amounted to a tremendous outpouring of information, the responses told of the frustrations of obtaining a diagnosis, of patients losing jobs and, oftentimes, benefits before a diagnosis was established, of the guilt which tore families apart when certain decisions were made, and of victims as well as caregivers fighting off alcoholism and depression. The investigators also found evidence of a wide variety of successful coping strategies: in some cases, those who responded felt the disease had acted as a catalyst in uniting the family; in other cases, family members became educators and advocates on behalf of patients. Once again, a major area of concern was the need for more information and emotional support from health professionals and others.

Samples of garden soil and drinking water in Guam, as well as in parts of Japan and New Guinea that are similarly plagued by high incidences of ALS and dementia, indicate low levels of calcium and magnesium and unusually high levels of aluminum. All of these elements have similar chemical structures. Scientists have never been able to prove that aluminum alone predisposes a person to, or causes, Alzheimer's disease. It may be that high intake of aluminum over a long period of time, coupled with chronic low intake of vital minerals such as calcium and magnesium, ultimately results in a breakdown of the normal mechanisms which metabolize minerals. This, in turn, could result in what investigators find are toxic levels of these elements in the brain cells and in the walls of major blood vessels in the brain. Scientists have yet to determine how or why low intake of calcium and magnesium can lead to high levels of these elements in the brain but there appears to be a link since the same phenomenon occurs in three different high incidence areas. Perhaps the body is overcompensating for the lack of vital minerals by storing these in combination with other available trace elements in the bones. Ultimately this may lead to deposits in the central nervous system.

NIMH scientists are also involved in studies of how aluminum gains access to the brain. During the past several years, researchers at the NIMH Adult Psychiatry Branch at St. Elizabeths Hospital in Washington, D.C. have measured the concentrations of aluminum and a variety of other minerals in the hair of Alzheimer patients and their healthy spouses. Examples of these minerals are calcium, magnesium, manganese, copper, and zinc. To date, no difference in any of the minerals studied have been found between the two groups. Further, serum copper and zinc have been examined in both groups. Again, no differences have been noted.

Future studies in this area will determine whether accumulations of metals in the brain are a primary cause of Alzheimer's disease or if other factors or circumstances might combine with environmental factors to trigger the onset of chronic, but ultimately fatal, diseases of the nervous system.

Slow Virus Studies

The quest for an understanding of what causes Alzheimer's disease continues with studies on central nervous system (CNS) diseases believed to be caused by slow-acting transmissible viruses.

Scrapie, a CNS disease that affects sheep, has provided a model for the study of dementing disorders in humans, including Alzheimer's disease. It is difficult to find an animal model for Alzheimer's disease, since dementia involves the loss of a capacity we cannot be sure animals ever had. Nonetheless, scientists are actively pursuing an animal or other model. Scrapie is similar to kuru and Creutzfeldt-Jakob disease, two rare diseases which cause progressive, irreversible dementia in humans. This fact, plus the well-established evidence that scrapie is the result of a slow-acting infectious agent, encouraged a new avenue of research on the possible causes of CNS disease in humans.

Scientists pursuing this line of research, however, have consistently failed in their efforts to identify and isolate any component of the infectious agent. Research at the University of California at San Francisco suggests that a protein is the vital force of the scrapie agent. NIA/NINCDS grantee Stanley B. Prusiner finds that animals with scrapie are infected by what he calls a small proteinaceous infectious particle, or "prion."[6] Prusiner's latest research tentatively suggests that the amyloid plaques seen in victims of Creutzfeldt-Jakob disease and kuru, two transmissible degenerative brain diseases, may be composed of prions. Amyloid plaques are also present in the Alzheimer brain.

Prions have many properties which distinguish them from typical viruses. Although viruses contain nucleic acids which carry all of the information necessary for the virus to multiply and spread infection, prions may or may not contain a nucleic acid. Since nucleic acids are necessary for proteins to replicate, this raises some exciting questions.

According to a study at the Philadelphia Geriatric Center, professionals from different clinical disciplines generally agree in the diagnosis of senile dementia. NIA grantee Samuel Granick has found that despite their dependence on the tools of their individual specialties, almost all of the clinicians involved in his research felt that severe memory loss, disorientation, and a decline in mental functions are the most distinctive symptoms of senile dementia. The physicians conducted extensive medical, social, and behavioral evaluations of 111 elderly volunteers.

As part of their research, Granick and his colleagues also developed a list of 141 medical and psychological factors which can be used to detect senile dementia in its earliest stages. This list included a few purely medical variables, such as a history of heart problems, which, according to the investigators, might distinguish individuals with moderate to severe forms of dementia from nondemented subjects if vascular dementia is the cause. None of these medical factors were sensitive enough to detect mild forms of dementia. On the other hand, tests which measured aspects of psychological function showed the extensive and seriously deteriorative effects of senile dementia. Combining tests even made it possible to single out patients who were only mildly affected. According to Granick, performance on behavioral or psychological tests would appear to be more useful than the standard medical measures currently used in the diagnosis of senile dementia.

Granick further refined his list of factors and came up with 15 variables—most of which deal with the quality of intellectual function—which together can serve as a basis for diagnosis. Using a step-by-step process to measure such functions as mental status and memory, Granick accurately classified 93 percent of a smaller group of volunteers in the study as either mildly demented, suffering from moderate to severe dementia, or nondemented. Since there has never been a single reliable and valid test to diagnose senile dementia in its earliest stages, such work by behavioral scientists may someday prove extremely useful to physicians.

Family Studies

In addition to studying the mechanisms and cause(s) of Alzheimer's disease, research scientists have begun to take a closer look at the families of Alzheimer victims. Alternately parallelling, inspiring, and building upon the development of family support groups, these studies have uncovered some intriguing findings about how families cope and how to help them cope.

Bayles' study is one of several looking at the language skills of healthy aged adults and what happens to these skills when subjects suffer from Alzheimer's disease, Huntington's disease, Parkinson's disease, or multi-infarct dementia. Her results confirm that patients in all stages of dementia have difficulties expressing themselves, but also suggest that tests of language skills are sometimes more sensitive than certain psychological tests to the presence of dementia. Although her studies are not yet completed, it appears that the deterioration of language skills is more severe and more rapid in Alzheimer's disease than in other forms of irreversible dementia.

As this study progresses, Bayles and her colleagues hope to develop a standard against which health professionals can measure the verbal performance of their patients. According to Bayles, tests of linguistic skills might be refined to determine the presence and severity of senile dementia and to outline interventions that might improve comprehension. She has already found a certain logic in the incorrect responses given by Alzheimer patients: moderately affected patients who cannot name a given object often will substitute a word which describes the object or the name of a similar object. At the very least, such studies might provide valuable information on the best methods for communicating with patients over the course of a disease which progressively limits communication.

Diagnosis of Alzheimer's Disease

What happens when an older person starts to show signs of "senility"? With luck, someone—perhaps a relative—will realize the importance of going to a physician to find out what is causing the problem, if it is curable and, if it is not, what can be done to help. The victim's first contact with a health professional is likely to be an internist, a geriatrician, or a general practitioner. Because of the variety of conditions that can cause what is medically known as senile dementia—and also because of the wide range of symptoms—the patient may eventually consult or be examined by a neurologist, a psychiatrist, a psychologist, a radiologist, and/or a social worker. In this way, the family might be exposed to the terminologies used by various specialists: senile dementia, Alzheimer's disease, organic brain syndrome, brain failure, and senile psychosis. The accurate diagnosis of "senility," by whatever name, is clearly a challenge for physicians.

Prusiner's work remains to be confirmed, but if it is, it might significantly alter our understanding of the nature of this virus and how it works with possible implications for CNS degenerative disorders such as Alzheimer's disease.

Related Research

The National Institute of Allergy and Infectious Diseases (NIAID) conducts research on the biology and epidemiology of viruses associated with persistent and latent infections. William J. Hadlow and his colleagues at the NIAID Rocky Mountain Laboratories have studied Suffolk sheep naturally infected with scrapie virus and have outlined the main events in the infectious process. They found the virus in such lymphatic tissues as tonsils and in the intestines of clinically normal lambs, aged 10 to 14 months, whose mothers later developed the symptoms of scrapie. As the lambs grew older, virus was found in the brains and spinal cords. These findings suggest that primary infection occurs by way of the digestive tract, either before birth from virus in amniotic fluid or after birth from virus in a contaminated environment.

Hadlow's study on scrapie may have implications for Creutzfeldt-Jakob disease, providing clues not only to its cause and development, but also to its possible links with exposure to the scrapie virus. For example, many investigators have looked for some association with eating sheep brain. But this study shows that virus is not present in the brains of young lambs, those most often used for human food, and underscores the importance of further research.

Since the central nervous system is susceptible to viral infections, research on these diseases may eventually provide a key to understanding currently baffling degenerative diseases such as Alzheimer's disease.

Immunological Studies

NINCDS-supported investigators at Sloan-Kettering Institute for Cancer Research are exploring the relationship between changes in the immune system and central nervous system disease. Research in patients who have a specific immune system deficiency has linked dietary intake to immune mechanisms. Previous studies have examined this relationship in cardiovascular disease. Investigators are now attempting to elucidate immunologic mechanisms in such chronic degenerative disorders as Alzheimer's disease.

Genetic Studies

For several decades, research on Alzheimer's disease has hinted that in either its early onset or senile form, the disease might be hereditary. In what amounts to a handful of studies on genetic influence, researchers have found an increased incidence of some form of dementia among parents and siblings of victims. Some studies show a slight increase; others show a considerable one over the occurrence of dementia in the general population. One researcher has suggested that early onset Alzheimer's disease poses a greater risk to relatives than late onset disease. Practically no data are available on risk to children. Briefly stated, the studies show a clustering of dementia cases in some families but no consistent pattern of genetic transmission.

Genetic research may eventually tell us whether we are dealing with one disease or more in the presenile and senile forms of Alzheimer's disease. Such studies may also provide a way to diagnose dementia accurately using a "marker" for the disease. At the Brentwood VA Medical Center and the UCLA School of Medicine, Lissy Jarvik and her colleagues have found something unusual in the behavior of white blood cells taken from patients with Alzheimer's disease.[7] With support from NIMH, Jarvik plans to continue to study what she describes as the "disoriented" behavior of cells from Alzheimer patients when exposed to temperatures which generally elicit a specific response from cells from healthy individuals. Future research from this laboratory will attempt to determine if this change is consistent and what causes it.



Psychosocial Research

Little research has so far addressed whether psychosocial factors (e.g., environmental stressors, depressive states, alcoholism) might contribute to the cause or development of Alzheimer's disease. To date, behavioral science research has focused mainly on the search for definitive diagnostic tests, including tests which will differentiate between Alzheimer's disease and multi-infarct (vascular) dementia; on changes in language use in relation to brain function and dysfunction; and on special supports needed by families of victims.

Language Usage

General difficulties in language usage and comprehension have always been included among the symptoms of Alzheimer's disease and other irreversible dementias. Now, an NIA-supported research scientist finds that specific language problems might be used to detect and diagnose various forms of dementia.

The recommended examination of an older person complaining of memory loss and confusion includes a battery of physical and neurological tests as well as certain psychological tests to detect or monitor declining skills. Commonly used tests can quickly evaluate a person's sense of time, place, and self. They can also assess short-term memory as well as the person's ability to complete simple mathematical calculations, both of which are among the first clinical signs of Alzheimer's disease. More and more, however, mental status tests include questions aimed at evaluating language skills. A patient will be asked to name objects, exhibit comprehension of a spoken or written statement, or write a spontaneous sentence.

Kathryn Bayles, an NIA grantee at the University of Arizona, has found that asking subjects to name common household or everyday objects—such as a broom, a purse, an apple, or a telephone—can easily differentiate between moderately impaired Alzheimer patients and healthy older individuals, and in some cases can detect mild cases of Alzheimer's disease.[8] Such demands can uncover the subtle, if serious, deficiencies often masked by the residual social skills of an Alzheimer patient in early and middle stages of the disease.

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Dear Mr. Wallace:

The NIA is involved in a number of exciting activities related to Alzheimer's disease that may not be reflected in this material... including a national education center that may be awarded before the end of the summer.

Please let me know if there is anything more I can do to help you.

Marian Emr
496-1752

National Institute on Aging
NIH Publication No. 86-2873
December 1986

PROGRESS REPORT ON ALZHEIMER DISEASE: Volume III



U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
National Institutes of Health

Introduction

We know many things about Alzheimer disease that we didn't know a decade ago. More physicians know it when they see it; they even know how to treat some of its less serious symptoms, but they don't know how to stop it from getting worse or how to cure it. Scientists know more about what goes on inside the brains and bodies of people who have it, but they still don't know what causes it. Policymakers know that more and more people have it, that the numbers are likely to increase as life expectancy increases, and that the cost of their care could bankrupt a small nation in the years to come if nothing is done about it. Victims and their relatives now know better where they can go for help, but most cannot afford the cost of care. And the general public knows it exists . . . which is more than they knew a decade ago.

This report is intended to summarize advances in our understanding of the major cause of mental disability among older Americans.

Demography

By most estimates, Alzheimer disease is the cause of serious confusion and forgetfulness in some 2.5 million American adults. This is five times the estimate that appeared in the literature 10 years ago when the National Institute on Aging (NIA) began its first studies in this area. Are there so many more victims now than then? Is there an Alzheimer epidemic?

Because aging is the principal risk factor associated with Alzheimer disease, the number of Alzheimer patients is growing at least as fast as the U.S. older population. But these latest estimates stand for more than just growing numbers of older people. They reflect a more sophisticated, if not yet perfected, approach to diagnosis; better training of health care professionals regarding the problems of old age; and the general public's greater awareness of Alzheimer disease and its symptoms.

According to NIA-supported experts at Harvard University, our current estimates of the number of people with Alzheimer disease may still be too conservative. Dr. Denis Evans and his colleagues at the East Boston Neighborhood Health Center have examined the residents of that Boston community and have found that more than 11 percent of the population over age 65 may be suffering from Alzheimer disease. This is double the frequently stated estimates.

When this study has been completed and verified by other studies, and diagnostic capabilities are further refined, we may be surprised to learn how many people are suffering from Alzheimer disease and are being quietly cared for by relatives and friends.

The Cost of Alzheimer Disease

According to the Alzheimer's Disease and Related Disorders Association, $35 billion was spent last year on the care of Alzheimer patients. This includes the costs of nursing home and other long-term medical care, but doesn't begin to account for the emotional and social costs of the disease.

NIA health economist Dr. William Cartwright has tallied some of the specific costs of Alzheimer disease, suggesting that $35 billion is just the tip of the iceberg. Dr. Cartwright and his colleagues, Dr. Lien-Fu Huang of Howard University in Washington, D.C., and Dr. Teh-wei Hu of Pennsylvania State University in State College, estimate

that the special services required by dementia patients might cost more than $38 billion, with another $39 billion for what the investigators call indirect costs.

The investigators looked at how much money is spent on longer hospital stays, increased need for drugs, greater demands on staff time in nursing homes, special social services and other needs. A large portion of the cost of dementia—$27 billion—reflects the value of the time spent by relatives who care for Alzheimer patients at home.

This is the first time that anyone has calculated the costs of dementia. It is also the first time that anyone has put a value on the so-called "incalculable costs" of the disease. The $39 billion for indirect costs represents the investigators' estimate of the cost of relatives visiting patients in nursing homes, transporting patients for needed medical services, and premature death due to dementia. Dr. Cartwright cautions that these estimates may seem conservative because they include only the extra costs of medical care, rather than all the costs of medical care, for dementia patients.

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Washington, D.C. 20402

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Diagnosis

There is no single medical test that can diagnose Alzheimer disease. The early symptoms of Alzheimer disease—forgetfulness, confusion, changes in mood and behavior—are also symptoms of a large number of other conditions. As a result, physicians who suspect Alzheimer disease use a variety of tests, including medical history, clinical examination, blood and other laboratory tests, psychological tests and radiologic scans. The diagnosis of Alzheimer disease is made only after all other possibilities have been excluded.

Nonetheless, we are better able to diagnose Alzheimer disease today than ever before. Physicians are more attuned to the various disorders that can mimic Alzheimer disease, and are more likely to detect them during medical examinations. Newer psychological tests have begun to focus more closely on the early and progressive signs of Alzheimer disease. And now, recent developments in radiology have provided diagnostic tools that can better visualize the working human brain.

At the Massachusetts General Hospital in Boston, NIA grantee Dr. John Growdon and his colleagues are using magnetic resonance imaging (MRI), a recently developed diagnostic tool, to examine patients with Alzheimer disease and other forms of dementia. For an MRI scan, the patient is positioned inside a magnetic field crossed by radio frequency waves. The magnetic field causes the body's abundant supply of hydrogen atoms (which are positively charged) to come into alignment; the radio waves then deflect them out of alignment. When the waves are turned off, computers measure the energy emitted as the atoms realign within the magnetic field. By a complex system of calculations, information is then generated on the concentration of matter as well as certain physical and chemical properties.

The technique is safe and painless. In some cases, MRI brain scans may even be superior to CT scans in that the images are crisper, they differentiate between white and grey matter and they can visualize deep areas of the brain not seen in CT scans. Because MRI can more accurately pinpoint tumors and other intracranial disorders, the scans are extremely useful to physicians in diagnosing patients' problems.

Dr. Growdon and his colleagues have found that the unique ability of MRI to distinguish the brain's white and grey matter allows it to pick up abnormalities that may indicate early multi-infarct dementia, or MID (dementia caused by a series of small strokes). MID is the second leading cause of dementia in older people and is frequently

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AGING UPDATE

From the National Institute on Aging
Bethesda, Maryland 20205

Research Update/ May 1, 1987:
Scientists Highlight New Promise In the Diagnosis of Alzheimer Disease

Since the mid 1970's, scientists have focused on the microscopic changes that take place in the Alzheimer brain for clues about the disease and its causes. They've looked at the jumbled masses of protein fibers that make up neurofibrillary tangles, at the degenerated nerve cell endings that form the characteristic neuritic plaques, and at the amyloid protein that collects at the center of the plaques. In the past six months, NIA-supported studies of these nerve cell changes have begun to reveal differences that may be useful in the diagnosis of the disease.

Dr. Peter Davies and other scientists at the Albert Einstein College of Medicine in the New York City are on the trail of unique abnormalities that may serve as markers for diagnosing Alzheimer disease. Using an antibody they have produced and named "Alz-50," Dr. Davies and his colleagues have discovered an abnormal protein, which they call A-68, that is abundant in Alzheimer brains but absent in normal brains. Interestingly, the protein was most evident in those areas of the Alzheimer brain that suffer significant

cell loss. However, in some cases it appeared before the disease's damage became apparent.

Although Dr. Davies found A-68 throughout the diseased nerve cells, most of it was concentrated in the neuritic plaques. Most recently, the scientists found A-68 in the cerebrospinal fluid of eight of nine patients with presumptive diagnoses of Alzheimer disease, and in none of twelve healthy individuals. If this work is corroborated by others, it may allow diagnosis through lumbar puncture. If A-68 is found in the blood of Alzheimer patients, it could lead to an even more valuable diagnostic tool.

Other exciting findings have been reported in the field of molecular genetics. National Institutes of Health scientists have isolated the gene that they believe to be responsible for the production of the amyloid protein found in damaged areas of the Alzheimer brain. Perhaps more significantly, these scientists, working in conjunction with NIA grantees and a group of French scientists, have recently found that familial Alzheimer patients, non-familial Alzheimer patients, and patients with Down syndrome all have an abnormal number of copies of this gene on chromosome 21, the same chromosome that seems to be responsible for Down syndrome. These findings add weight to other evidence of a link between Alzheimer disease and Down syndrome, and substantiate the theory that Alzheimer disease is at least, in part, a hereditary affliction.

Whether the amyloid gene and the familial "Alzheimer gene" are the same or only in close proximity remains to be established. These studies, however, may be instrumental in locating the site of a gene that might cause Alzheimer disease, identifying those at risk for the disease, and perhaps someday a therapy for the disease based on correcting a genetic defect.

Alzheimer Disease Research Center Program

The National Institute on Aging currently funds 10 Alzheimer Disease Research Centers (ADRC's) in a program designed to speed us toward an understanding of what causes the disease and what can be done to treat it. Research topics range from studies of the basic mechanisms of Alzheimer disease to those aimed at managing the symptoms and helping families to cope, with each of the 10 centers having its own unique areas of emphasis.

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confused with Alzheimer disease because of similar symptoms.

Whether MRI will be a valuable diagnostic tool for Alzheimer disease is difficult to predict since this technology is still in its infancy. In the meantime, however, Dr. Growdon and his colleagues are excited by their findings of white matter lesions in people who show no other sign of disease. If this is, indeed, an early indication of multi-infarct disease, diet and lifestyle changes may prevent further damage.

As this research progresses, Dr. Growdon will be looking at those areas of the brain known to be affected in Alzheimer disease to see if changes in brain structure can be linked to changes in function as the disease progresses.

A Blood Test for Alzheimer Disease?

While MRI might eventually prove useful in differential diagnosis, a number of studies are holding out the hope of a simple diagnostic test for Alzheimer disease. Anatomically, Alzheimer disease is characterized by neurofibrillary tangles and neuritic plaques, as well as by deposits of amyloid fibers in the brain's blood supply. Dr. George Glenner at the University of California, San Diego has isolated and analyzed the amyloid fibers circulating in the bloodstream of Alzheimer patients and found a unique protein not seen in healthy individuals. Interestingly, the same protein appears in the amyloid deposits of Down syndrome, representing a link between Alzheimer and Down syndrome. With NIA support, Dr. Glenner next plans to use monoclonal antibodies to take a closer look at this unique protein with the hope of isolating its precursor.

This is one of several studies looking at proteins that can be linked to what takes place in an Alzheimer patient's brain as nerve cells begin to die. In studies at the Albert Einstein College of Medicine in the Bronx, New York, scientists have discovered an abnormal protein which they say is found only in the brains of Alzheimer patients, and only in those parts of the brain that are most severely affected by the disease. At Brigham and Women's Hospital in Boston, Massachusetts and the New York State Institute for Basic Research in Staten Island, other scientists have found that a normal protein is somehow altered during the course of Alzheimer disease, and speculate that this may play a role in the death of nerve cells. If scientists can find these same proteins or related proteins in the bloodstream or in some other body fluid, we may soon have a simple diagnostic test for Alzheimer disease.

Biological Mechanisms

In a series of investigations supported by the NIA, Drs. Charles Marotta and Elizabeth Sajdel-Sulkowska of Harvard Medical School and McLean Hospital in Belmont, Massachusetts have found a biochemical abnormality that impedes production of new protein in Alzheimer brain tissue.

For some time we have known that the most serious symptoms of the disease are closely correlated with the intracellular accumulation of abnormal protein structures called neurofibrillary tangles. But scientists have always been puzzled as to how these pathological changes relate to normal cell function.

Drs. Marotta and Sajdel-Sulkowska compared autopsied tissue from the cortex of six Alzheimer patients with that from four patients of the same ages who died of other causes. In the diseased brains, the investigators found massive accumulations of neurofibrillary tangles and little more than half the normal amounts of ribonucleic acid (RNA). RNA is a key chemical in the production of protein, a process that is critical to the life of the cell. A closer look linked the lower levels of RNA to the presence of increased ribonuclease activity. In the healthy brain, ribonuclease breaks down RNA, but its activity is closely controlled by an inhibitor protein. In the Alzheimer brain, Drs. Marotta and Sajdel-Sulkowska found that ribonuclease activity was higher, resulting in more destruction of vitally important RNA which results in less protein synthesis.

This work is an extension of earlier studies in which Dr. Marotta and his colleagues first showed that messenger RNA can be removed from the postmortem brain for scientific study. Until Dr. Marotta's pioneering work, it had been assumed that large molecules such as RNA and deoxyribonucleic acid (DNA) were broken down very quickly after death. This might have been the case using more traditional chemical methods for storing brain tissue. Formalin, the chemical used to fix brain tissue after death, destroys enzymes and other fragile biochemical substances in the autopsied brain. But most of these problems are alleviated when autopsied brain tissue is frozen and later thawed for study. According to Dr. Marotta, if the brain has been frozen and stored, RNA will synthesize protein as if in a living brain, even years after death.

As the investigators are quick to point out, their work on autopsied brain tissue has already been corroborated in living patients. Using positron emission tomography, a noninvasive technique which

Conclusion

The National Institute on Aging hopes to continue to expand its research on Alzheimer disease. Studies will focus on analyzing the protein chemistry of normal and abnormal brain structures; developing monoclonal antibodies for specific brain proteins; looking at brain enzymes, particularly those related to oxidative metabolism and neurotransmitter synthesis; and measuring the effects of toxins, infectious agents and genetic factors on brain degeneration. NIA will continue to support research on ways to make an early and accurate diagnosis of Alzheimer disease, and to use improved diagnosis as the basis for establishing multinational epidemiologic studies. Through a cooperative arrangement with NINCDS, NIA will provide cells from definitely diagnosed Alzheimer cases to investigators studying the molecular biology and genetics of the disease. We also hope to expand research on the behavioral and social aspects of the disease, including how families cope under such tremendous stress.

In 1984, the NIA was authorized by the U.S. Congress to establish Alzheimer Disease Research Centers, 10 of which are currently being funded. The most exciting opportunity for future research on Alzheimer disease rests in the potential of these centers to act as a network for sharing new ideas as well as research results. Already, the center directors are communicating about such matters as joint patient registries; shared data, tissue, and brain banks; and standardized diagnostic criteria. The Alzheimer Disease Research Centers share a common goal: to enhance research on the disease by providing the resources and environment for collaborative studies among many scientists from many different disciplines. The long-term reward may be a way to cure and possibly prevent Alzheimer disease. The immediate payoff will be better care for more of its victims.

Previous studies at the Mount Sinai GCRC and other medical centers had indicated that intravenous use of the drug temporarily improved the memory of Alzheimer patients. Uniform levels of physostigmine, however, were difficult to maintain due to its short (30-minute) half-life in the bloodstream. Other tests had indicated that a constant level of the drug may be achieved if it is taken orally every 2 hours. The investigators found varying improvements in the memory, sleeping patterns, and behavior of Alzheimer patients during two studies with the drug.

In the first study, designed to find the most effective dose of physostigmine, 10 of the 12 patients significantly improved their scores on the Alzheimer Disease Assessment Scale, the evaluative test described above. But in a followup test that compared a placebo with the physostigmine dose believed to be most effective, only three patients showed significant improvement using physostigmine; four others improved slightly.

According to Dr. Mohs, drugs that increase acetylcholine activity may help some patients with Alzheimer disease, but further research is needed to identify safer, longer-acting drugs.

monitors metabolic activity in living brain tissue, a group of French scientists has found a 65 percent drop in brain protein synthesis in patients in the later stages of Alzheimer disease.

It is not possible to state if this change marks the onset of Alzheimer disease, or if it is just one of a series of events that takes place as brain cells begin to die. If, as the investigators speculate, decreased protein synthesis results in the chemical changes and brain cell death characteristic of Alzheimer disease, then we might be one step closer to finding out what causes this debilitating illness.

Changes in Brain Chemistry

In addition to the accumulation of neurofibrillary tangles in the Alzheimer brain, another hallmark of the disease is a disruption of one of the brain's chemical messenger systems, the cholinergic system. With support from the National Institute of Neurological and Communicative Disorders and Stroke (NINCDS), Dr. Joseph Coyle and his colleagues at The Johns Hopkins University in Baltimore, Maryland, have shown that one message pathway in the cholinergic system that deteriorates in the brains of Alzheimer patients also is destroyed in a rat model. This discovery might help explain why the brain's cortex and hippocampus, which lie at the end of this pathway, accumulate tangles and plaques, and why Alzheimer patients lose short-term memory governed by the cholinergic system but retain the long-term memory maintained by other chemical messenger systems.

Dr. Coyle has simulated cholinergic system deterioration in rats using a chemical that damages only cholinergic neurons. His study suggests that memory loss in the rat model of Alzheimer disease may be reversible: animals with induced cholinergic damage eventually regained some of their short-term memory.

In yet another study, NIA/NINCDS grantee Dr. Marek-Marsel Mesulam and his colleagues at Beth Israel Hospital in Boston, Massachusetts, have identified a distinct group of cholinergic neurons extending from the basal forebrain along cholinergic pathways and linking selected neurons in the basal forebrain with particular regions in the cortex. The investigators previously had demonstrated that changes in such cell groups can trigger the kind of brain dysfunction associated with Alzheimer disease. Studies of the newly discovered cell group show that these cells influence a region of the brain that transmits visual and other sensory information.

The Search for a Cause

The theories of what causes Alzheimer disease have matured in a rich atmosphere of research focused on the neuroscience of aging. The basic theories have not changed. Scientists still think that genetic factors; immunologic changes; unconventional virus-like agents; and environmental factors may all play a role in the development of Alzheimer disease. Nonetheless, more basic answers are being sought as to what causes the disease. NIA-supported scientists are examining the fundamental processes that underlie changes that take place in the brains of patients with Alzheimer disease.

At the Burke Rehabilitation Center in White Plains, New York, NIA grantee Dr. John Blass and his colleagues are doing research on enzyme activity, calcium transport, glucose metabolism and protein synthesis in an effort to reveal the events that precipitate neurotransmitter changes and even cell death in Alzheimer disease. Their search has led them to look at tissues, fluids, and cells outside the brain. Based on their results, they have speculated that Alzheimer disease is a systemic metabolic disease, not simply a neurologic disorder.

For some time, scientists have known that there is a drop in overall glucose metabolism in the brains of Alzheimer patients; in other words, the Alzheimer brain uses less energy. Dr. Blass and his colleagues looked at glucose metabolism in tissues taken from Alzheimer patients and found that there was an inherent abnormality in the cells' ability to break down glucose into energy. They also found a defect in calcium transport at the cellular level.

According to Dr. Blass, Alzheimer disease may be a neurologic disease with systemic manifestations or a systemic disease that shows itself primarily in terms of brain changes. This realization may alter the approach to studies of how the disease develops and how it can be diagnosed and treated.

Alzheimer and Pick Disease: A Common Cause?

Other research continues to alter our understanding of Alzheimer disease. At Harvard University, NIA grantee Dr. Dennis Selkoe has found a surprising similarity between Alzheimer disease and Pick disease, a rare, rapidly progressive dementia.

Assessment and Treatment

Several times during the past few years, the media have publicized major improvements in Alzheimer patients given experimental drugs. Each time, a closer examination has revealed that there is still a great deal of work to be done. Scientists now find it necessary to use a variety of tests to evaluate their patients' responses to new drugs, without knowing how reliable the tests results are. A pressing need is for a test that can be used to assess the potential of any drug.

At the Bronx Veterans Administration Medical Center in New York City, NIA grantee Dr. Kenneth Davis has devised a simple test that focuses on the major symptoms of Alzheimer disease and can be used to evaluate patients in all stages of the disease. The test is brief, easy to administer, and can be used anywhere the patient is located. It evaluates such factors as memory, language, mood and behavior; it rates the majority of the items on a five point scale of severity so that subtle changes can be detected.

Dr. Davis and his colleagues originally designed a scale with 40 items. After more than a year of tests, they have pared the list to 21 items they believe are valid and reliable measures of any change in a patient's symptoms of Alzheimer disease.

It is hoped that the Alzheimer Disease Assessment Scale will be sensitive enough to measure the success of any future attempts to treat the disease.

Treatment Approaches

As noted above, patients with Alzheimer disease often have a marked reduction in cells that produce acetylcholine, one of the neurotransmitters that allows nerve fibers to send electrical messages. The loss of these cells may be a cause of some symptoms of the disease. In an effort to increase nerve cell activity associated with acetylcholine, Dr. Richard Mohs and his colleagues at the Mount Sinai School of Medicine in New York City gave 12 patients oral doses of the drug physostigmine, which mimics the action of the neurotransmitter. The tests were conducted in the Mount Sinai General Clinical Research Center (GCRC), one of 78 such centers supported by the National Institutes of Health's Division of Research Resources.

Both of these studies lend support to the position that genetic factors play a significant role in Alzheimer disease.

Risk Factors in Alzheimer Disease

A team of American and Italian investigators recently reported on the largest case-control study of Alzheimer risk factors, completing a 3-year collaborative effort of the Italian National Research Council and the NINCDS. The findings indicated that people whose brothers or sisters have any form of dementia may be 11 times more likely than others to develop Alzheimer disease. The study also provided some support for earlier observations that severe head trauma may be a risk factor for Alzheimer disease, and that babies born to mothers over age 40 may be at greater risk for dementia later in life.

This study, carried out at seven Italian medical centers under the Science and Technology Agreement between Italy and the United States, did not support risk factors suggested by earlier, smaller case-control studies: family history of Down syndrome, previous thyroid disease, exposure to aluminum or other toxins, allergies, previous surgical procedures, habits of smoking or drinking wine, or certain personality traits. The results did suggest that diagnoses of Alzheimer disease may vary greatly according to the patient's socioeconomic status, probably because mental impairment is more noticeable in people whose education or lifestyle reflects a certain degree of intellectual achievement.

In addition to their work on this project, NINCDS intramural investigator Dr. Bruce Schoenberg and his research team have reported on the occurrence of Alzheimer disease among the 24,000 residents of Copiah County, Mississippi. This landmark study measured the incidence and prevalence of various neurological disorders in a racially mixed population. The results demonstrated that the rate of Alzheimer disease is similar among both blacks and whites. Furthermore, twice as many women as men had Alzheimer disease, and the number of Alzheimer patients increased with advancing age, from 1 percent among people age 40 years and older to 7 percent among those 80 years and older. The range of other estimates of Alzheimer disease indicates that more research in different populations may be needed to establish firmly the incidence of the disease. Nonetheless, this study reconfirmed that aging is one of the major risk factors for Alzheimer disease.

Alzheimer and Pick diseases have always been presumed to be distinct neurological disorders. Although victims of both diseases suffer disabling dementia, neurofibrillary tangles and neuritic plaques are not found in the brains of individuals who had Pick disease. Only an autopsy can distinguish between the two diseases.

Earlier studies by other investigators had shown that both Alzheimer and Pick diseases affect the same parts of the brain. Research had even speculated that although the lesions of Pick and Alzheimer are different, they might be composed of the same abnormal proteins called paired helical filaments (PHF). Following these leads, Dr. Selkoe used a technique developed in his laboratory to study nerve cells from the brains of Alzheimer and Pick victims. He found that the PHF's once thought to be unique to Alzheimer disease were indeed located in the brain cells of Pick patients.

Dr. Selkoe speculates that Pick disease may be a variant of Alzheimer disease and that the two may share a common cause. This opens up a new field of investigation.

The Aluminum Story

When scientists first looked at the brains of Alzheimer patients, they found excessive levels of aluminum concentrated in dying brain cells. These findings led to fearful speculation by the public that Alzheimer disease could result from ingesting aluminum or using household products containing aluminum. Fortunately, epidemiologists have ruled out such a simple answer to what causes the disease, and our approach to studies of environmental risk factors has become much more sophisticated.

NIA grantee Dr. Bernardino Ghetti has confirmed that when the central nervous system is exposed to aluminum over long periods of time, the result is neurofibrillary degeneration and ultimately cell death. In his work at Indiana University School of Medicine in Indianapolis, Dr. Ghetti is beginning to elucidate the mechanisms by which aluminum causes nerve cell damage. He has found that aluminum binds to the protein calmodulin, impairing its ability to regulate calcium levels in the cell. Calcium is similar in structure to aluminum and is vital to the life of the cell but toxic in large quantities. According to Dr. Ghetti, the key to aluminum's deadly effect on nerve cells may be this breakdown of calcium metabolism at the cellular level.

The Role of Infectious Agents

Since the late 1960's, scientists have been exploring the role of infectious agents in several dementing disorders. Today, some scientists are still looking to see if such an agent might be implicated in Alzheimer disease. Dr. Stanley Prusiner of the University of California at San Francisco—a grantee of the NINCDS and the NIA—first identified the "prion," which causes some infections that reside within the body for years before producing symptoms, as well as a specific protein that is the major component of the prion. Dr. Prusiner's latest research suggests that the prion protein comes from a larger protein present in both normal and infected cells. In normal cells, the larger protein is completely broken down by enzymes; in infected cells, a defective breakdown leaves the prion intact. According to Dr. Prusiner, this prion aggregates to form a fibrous structure that resembles certain filaments found in the brains of Alzheimer patients. Dr. Prusiner is now trying to determine what might happen to change a normal cell into an infected cell and why it appears that the larger protein behaves differently in infected cells than in normal ones.

Related Research

The hypothesis that an infectious agent is the cause of Alzheimer disease is based in part on the known transmissibility of certain other degenerative brain diseases in both humans and animals.

One animal model is scrapie, a slowly progressive neurologic disease of sheep and goats. Scrapie, which can be transmitted to a variety of animal species including mice, hamsters, and mink, is so named because stricken animals repetitively scrape against fence posts and trees. As the disease progresses, the animals degenerate steadily, become paralyzed, and die.

Scrapie infection is characterized by large fibril structures and neuritic plaques in brain tissue, features strikingly similar to pathologic findings in patients with Alzheimer disease. These plaques are found in many chronic diseases, although none has been detected so far in diseases in which viruses have been proven to be the cause.

Purified samples of scrapie-infected tissue have been shown to transmit disease to healthy laboratory animals. Upon close examination, the prion protein has been found to predominate in the infected tissue.

At the National Institute of Allergy and Infectious Diseases (NIAID) intramural Rocky Mountain Laboratories in Hamilton, Montana, Dr. Bruce Chesebro and his colleagues have discovered the genetic material for this prion protein in both healthy and scrapie-infected animals, indicating that the protein is probably a component of normal brain tissue.

Dr. Chesebro examined the brains and other organs of healthy and scrapie-infected mice, using a chemical probe designed to detect the messenger ribonucleic acid (mRNA) sequence that corresponds to the prion protein. Messenger RNA is the molecule that transmits the DNA message to the cell's cytoplasm where it directs protein synthesis. The mRNA sequences were found in tissues of both healthy and infected animals. In no case was the mRNA specific for scrapie-infected tissue.

Dr. Chesebro suggests that prions may simply be part of a healthy cell's structure, and some aspect of the infection causes the protein to bind together to form the deposits found in infected animals. In other words, accumulated protein may be the result of scrapie infection rather than the cause.

Dr. Chesebro's work does not explain the nature of the scrapie agent. His findings do make conceivable the theory that very small virus particles may be responsible for scrapie and other slowly developing diseases.

The Genetic Hypothesis

A discussion of possible causes of Alzheimer disease would not be complete without some reference to genetic studies. In an NINCDS-funded study of 3,500 nursing home residents, Dr. Marshall Folstein at The Johns Hopkins University found evidence of an autosomal dominant pattern of inheritance in certain families with high rates of Alzheimer disease. This could mean that each child of a parent with the familial form of Alzheimer disease has a 50 percent chance of developing the disease in later life.

It seems apparent from our research thus far, however, that the majority of Alzheimer victims don't inherit the disease from their parents. Despite evidence of a familial form of Alzheimer disease, it may be far more common for people to inherit a predisposition to the disease. In an NIA-supported study at the Bronx Veterans Administration Medical Center in New York City, Dr. John Breitner has found that Alzheimer patients are much more likely than those without the disease to have a close relative with dementia.

(Lange/Wallace)
April 24, 1989
7:30 p.m.
[CLEARWTR.DOC]

PRESIDENTIAL REMARKS: DEDICATION, ALZHEIMER'S CENTER
PALM HARBOR, FLORIDA
THURSDAY, APRIL 27, 1989
1:50 P.M.

Advance
7505

((Thank you, Mike [Congressman Bilirakis]... You know, in a little town near here, a guy got the attention of the local fish and game warden. Seems he brought in a huge catch, every time he went out on the lake. So the warden asks if he can go along with him, the next time. The guy says, "Sure."

So they get out there in the boat early one morning, and the guy reaches into his tackle box, pulls out a stick of dynamite, lights it, and throws it over the side. There's a big explosion under water -- and a dozen fish float to the surface.

The warden yells at him, "Don't you know that's illegal?" Well, the guy reaches down, pulls out another stick of dynamite, lights it, hands it to the warden, and says, "You want to argue? Or you want to fish?"))

Well, you didn't send anyone to Washington to argue. Or to fish -- although I do love fishing in the warm waters of the Florida coast. No, you sent us to Washington to find solutions. And ~~Congressman~~ Mike Bilirakis has been finding solutions and support

for Alzheimer's patients. For his work, we are all grateful.

It's a special honor to be here, on behalf of a cause that matters so deeply, to so many. Alzheimer's Disease extracts a devastating toll on its victims -- and on those who love them. By the time this century ends, nearly one out of four Americans will be over 50 -- and will face some risk of being striken with this disease.

The Michael Bilirakis Alzheimer's Center is ~~the first facility in the nation~~ designed to care for Alzheimer's patients -- all the way from diagnosis, to caring for them in their final days. This center will serve as a place of hope, and a source of comfort, until a cure is found.

While the disease may ravage its victims, it makes heroes and heroines of all who care for them. It may challenge the very fabric of the family -- but it demands new strength, a strength in each other that we might not have known we had.

But above all, this disease is a reminder of what ought to be an American birthright: that we should be able to live out our lives as engaged, productive, and full participants in this community of citizens.

In a nation that looks after its own, that birthright

entails its own responsibility: That any definition of a successful life must include serving others. That success is not, cannot be measured by the sum of our possessions, but by the good we do for others. That whatever life, and health, and love we have within us, we must share with others.

Older Americans represent a phenomenal reserve of talent and experience -- qualities this country can use right now. So even as I join you in dedicating a place of refuge and comfort for those stricken with a deadly disease, I would ask all of you who have the health and inclination, to consider how much we gain, when we give of ourselves.

Mrs. Bush's Office

In New York City, my wife Barbara met with a group helping young Cambodians learn English. While she was there, one older lady told Barbara how desperately lonely she had been, before she volunteered. Her eyes filled with tears at remembering it. And then her face lit up, as she told Barbara, "I've never been lonely a day since."

One person's need matches another's -- and a wonderful thing happens. I always like to remember that there is no exercise better for the human heart than reaching down, and lifting someone else up. The rest of your life really should be the best of your life.

At the Inaugural, I spoke of a new engagement in the lives of others. Today, I challenge those of you who can, to get involved -- and stay involved. Find a place, or an organization, or even a single life, where you can make a difference for someone else.

"The young know the rules," Oliver Wendell Holmes once said; "but the old know the exceptions." Many of you already <u>are</u> exceptions -- and exceptional. And I cheer you on.

Thank you. God bless you. And God bless America.

We're expanding on a Good Idea!

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2655 Nebraska Ave. (S.R. 584-A)
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Your Home with a Heart
...at the Heart of Pinellas

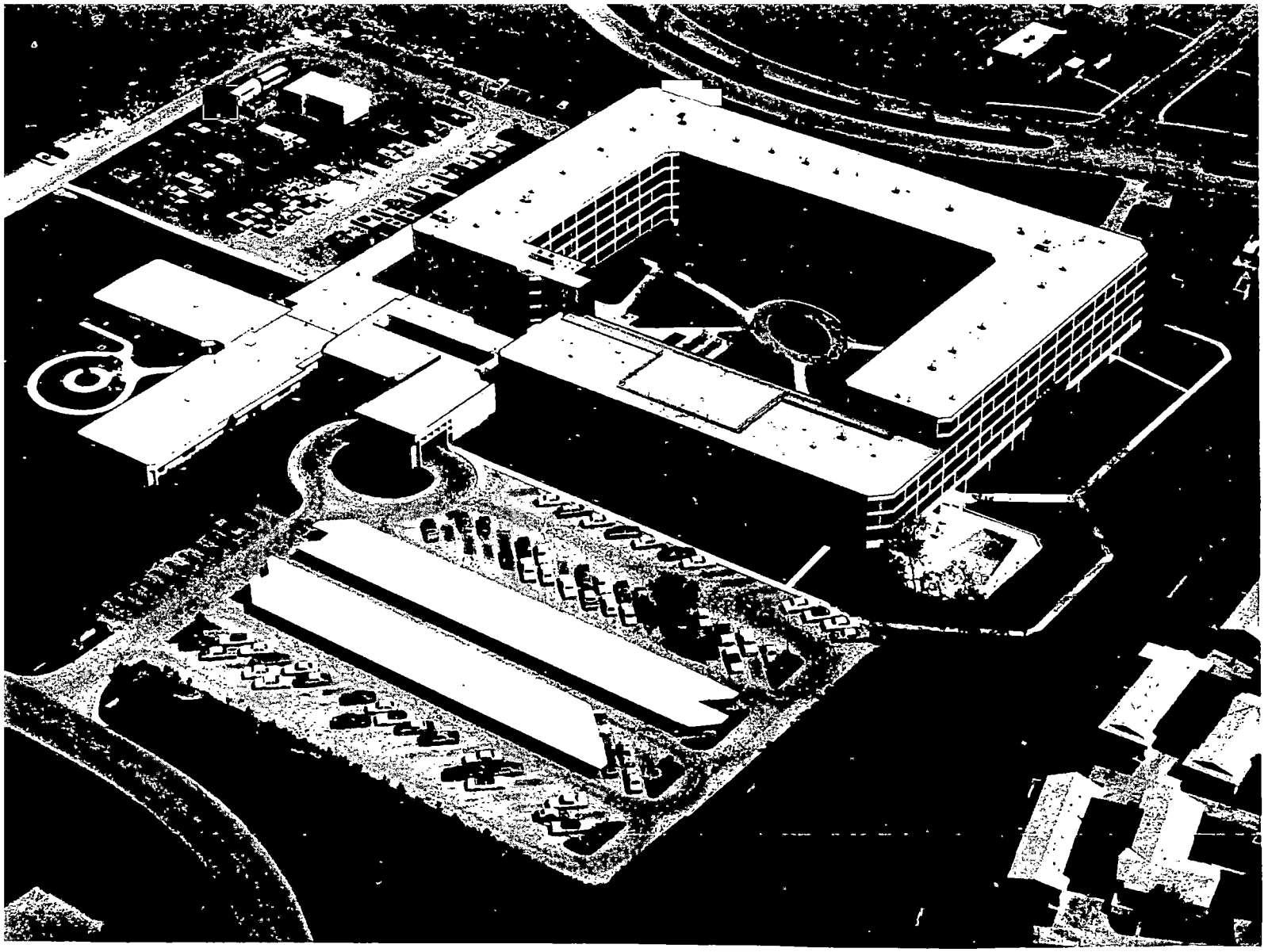
This unique retirement community is ideally located... in Palm Harbor, close to parks, beaches, golf courses, lakes and all the other advantages of highly-sought Pinellas County. The Village is only steps from supermarkets, drug stores and banks with Transit Authority buses at our corner and our own minibus for residents' use.

So the Village is not only an enormously enjoyable way to live, it's a wonderfully convenient place to live.

Come Join Us!

You are invited to share the freedom, fellowship and round-the-clock care enjoyed by the St. Mark Village family. Here clearly, is peace-of-mind for your ultimate years. Ask the Village office for application forms.

St. Mark Village
2655 Nebraska Ave. (S.R. 584-A), just east of U.S. 19
Palm Harbor, Florida 34684, Ph. 813/785-2576



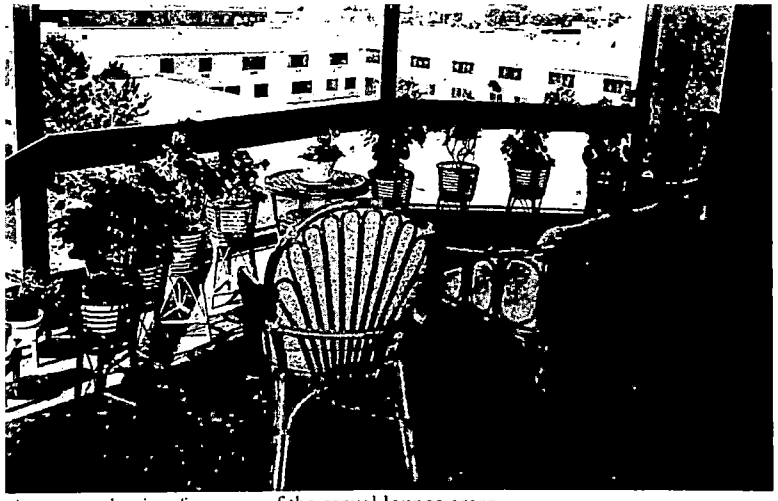
11.5 Acres of Amenities for your Luxurious Living... with safety, security and Round-the-Clock Christian Care

St. Mark Village is the fulfillment of dreams — yours and ours.

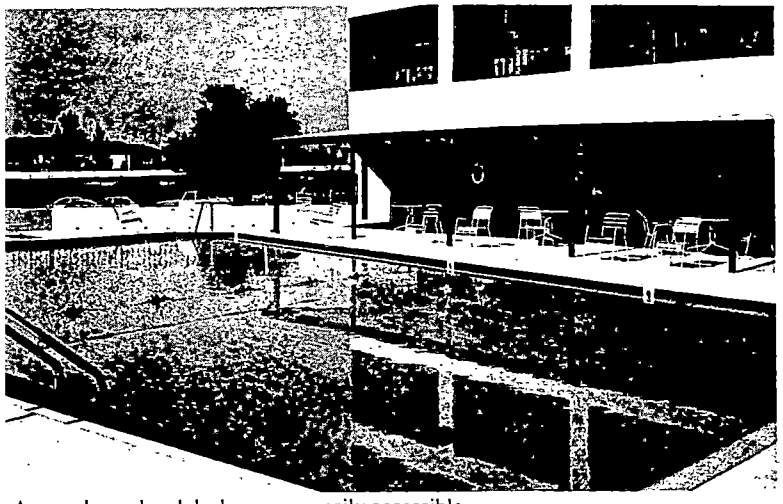
Your dream: to enjoy the rest of your life as the best of your life — with assurance your physical, social and spiritual needs will be answered. Our dream: to create a non-profit Christian retirement community providing this assurance in full.

The Village contains 324 deluxe studio, one bedroom and two bedroom apartments, each with a complete kitchen. Community facilities include the beautiful dining room (table service), spacious chapel, lovely lounges (and additional lounges on each floor), hobby and craft rooms, library, game rooms, heated swimming pool and whirlpool, shuffleboard, landscaped grounds.

The 60-bed Health Care Center provides ever-present professional attention. Thirty days care in the center is available to each resident per year without additional daily rate charge; additional time is at a discount. All Village apartments have direct emergency communication with the nursing center.



A panoramic view from one of the casual lounge areas.



An ample pool and deck area are easily accessible.



Your own private balcony.

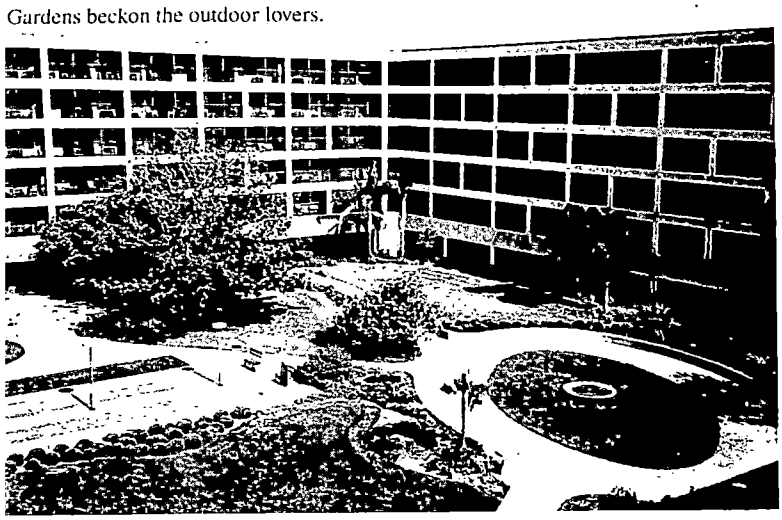
Enjoy these outstanding benefits and features at St. Mark Village

- Full meal daily served in dining room
- Weekly maid service
- All utilities furnished even local phone calls
- Soundproof and fireproof construction
- Complete all-electric kitchen including disposal
- Private balcony
- Individual heat and air-conditioning controls
- Carpeting and draperies
- Walk-in closets
- Luxurious lobby and lounges: laundry, storage rooms and lounges on each floor
- 3 resident elevators
- Reserved parking place
- Emergency nurse-call system
- Smoke and heat detectors
- Auxiliary power generator
- Security patrol
- Swimming pool
- Hi-temperature whirlpool
- Shuffleboard
- Men's Den with pool table
- Card and game rooms, library
- Craft, hobby and woodworking shops
- Social director
- Deluxe 60-bed nursing home
- 30 days in nursing center per person per year
- Day and night medical service and nursing staff
- Physical and rehabilitative therapy
- Dietician



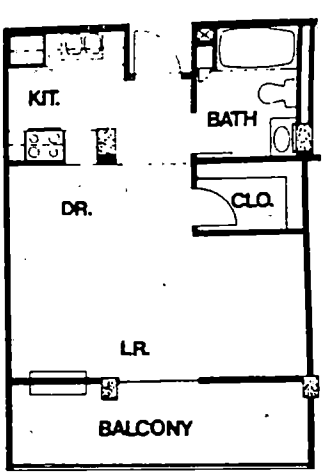
Bright, delightful dining room.

Gardens beckon the outdoor lovers.

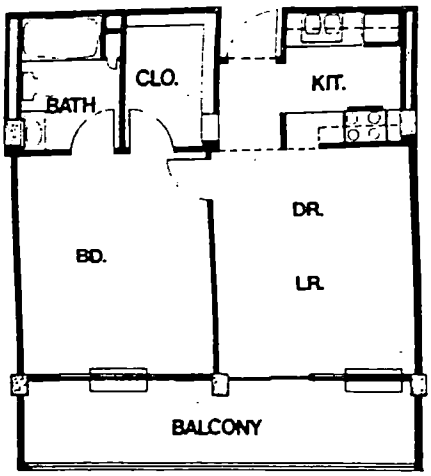


Friends, fellowship, food and fun.



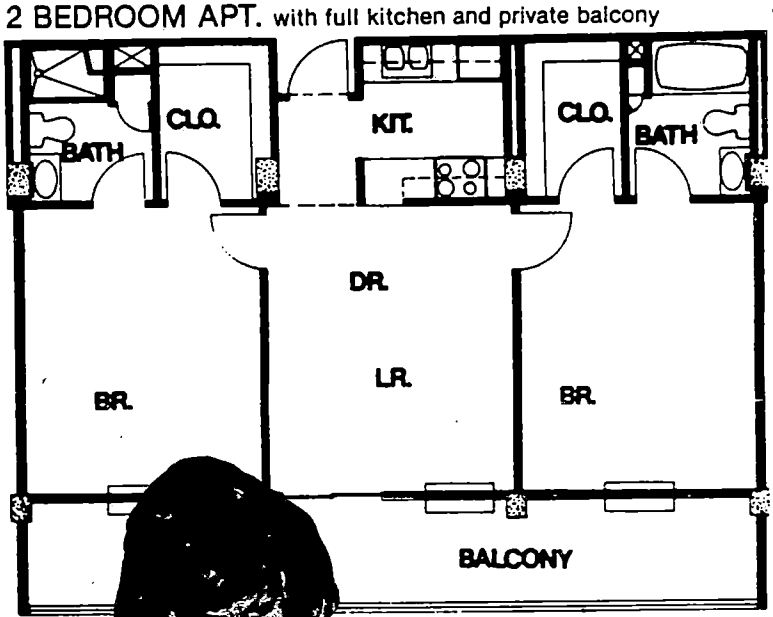


STUDIO APT.
with full kitchen
and private balcony



1 BEDROOM APT.
with full kitchen
and private balcony

2 BEDROOM APT. with full kitchen and private balcony



Complete range of conveniences.



St. Mark Village

YEURITH WAY
SALES COUNSELOR

St. Mark Village
P.O. Box 1449, Palm Harbor, FL 34682-1449
2655 Nebraska Ave., Palm Harbor, FL 34684
Telephone (813) 785-2577, Ext. 712

Enjoy these outstanding benefits and features at St. Mark Village

- Full meal daily served in dining room
- Weekly maid service
- All utilities furnished even local phone calls
- Soundproof and fireproof construction
- Complete all-electric kitchen including disposal
- Private balcony
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- Deluxe 60-bed nursing home
- 30 days in nursing center per person per year
- Day and night medical service and nursing staff
- Physical and rehabilitative therapy
- Dietician

"We're expanding on a Good Idea!"

St. Mark Village is a non-profit retirement community and health care center (nursing home) sponsored by St. Mark Lutheran Church, Dunedin, Florida, but entirely self-supported financially. Our mission is to provide superior living facilities as free of cares as it is possible for us to make them in an environment of Christian love and concern.

QUALIFICATIONS FOR RESIDENCY

St. Mark Village welcomes applications for Residents from active retired or semi-retired people who: (1) Seek deluxe apartment living free of maintenance and housekeeping drudgery with the security of around-the-clock communications with health care professionals; (2) Are 62 or more years of age, are ambulatory, able to live alone without assistance and are in reasonably good physical and mental health (when double occupancy is involved each person must meet these standards); (3) Are of good moral character; (4) Are financially able to meet the charges related to the accommodations occupied as well as their supplementary personal needs.

RESIDENTIAL FACILITIES AND SERVICES

Payment of the Admission Fee and the regular residential Monthly Service Fee provides a residential unit with kitchen, wall-to-wall carpeting, drapes, screened balcony, weekly maid service, maintenance, utilities including heat, air conditioning and local telephone calls, central TV antenna connection, one meal per day served in the dining room and scheduled minibus service.

Spiritual, social and recreational activities are available. Lobbies, lounges, public balconies and patios, an ice cream parlor, a beauty shop, conference room, chapel, arts and crafts room, and game room are all available for your use and enjoyment. Private dining rooms are available for special occasions at a nominal fee. Outdoor facilities in the landscaped grounds include shuffleboard courts, a swimming pool and high temperature whirlpool spa. You will be assigned your own parking space for your car.

Your own private balcony.

The Health Care Center is available for certain out-patient services at a nominal charge as well as in-patient care. Nursing services are available for emergency assistance 24 hours a day. Emergency signalling from your bedroom and bathroom are available if you are unable to telephone for assistance. If you don't make routine appearances such as for meals, we will check to learn if you are well.

APPLICATION FOR ADMISSION

When you have selected the unit you prefer, you will be given application forms which include: 1) Deposit — your application must include a deposit of 10% of the Admission Fee. If your application is not approved, this deposit will be refunded in full. Checks for deposit toward the Admission Fee should be made payable to the First National Bank of Clearwater, Trustee for St. Mark Village, Inc., (2) Minister's statement — a letter of character reference must be completed by your pastor and returned by him directly to St. Mark Village. (3) Personal information — personal and financial information is kept in strict confidence. The Minister's Statement and Personal Information forms should be returned to us as soon as possible for consideration by the Acceptance Committee. (4) Processing — completed applications usually can be processed within 2 weeks or less after we receive them. You will be advised immediately of the action of our Admissions Committee.

ADMISSION FEE

Ten percent of the Admission Fee is required at the time of your initial application. The balance will be due thirty days after notice to you that the residential unit will be ready for occupancy, or upon your taking occupancy, whichever comes first. If you withdraw your application after approval, but before occupancy, the Admission Fee or portion of the Fee you have paid will be refunded less a processing fee of 4% of the full Admission Fee.

Our refund policy provides a "trial period" of four years. If you decide to leave St. Mark Village during that time, the Admission Fee will be refunded less a 4% processing fee and less 2% per month for each month or fraction of a month you have lived here.

MONTHLY SERVICE FEE

The Monthly Service Fee is billed in advance and payable monthly on the date of occupancy or thirty days after notice to you that the residential unit is ready for occupancy, whichever occurs first. If you are away from St. Mark Village for thirty consecutive days or more, an absentee credit will be allowed against the monthly service fee (based on reduced food service only).

Although subject to adjustment, the Monthly Fees will be maintained at the lowest possible rate consistent with sound financial practices and maintenance of the quality and services to which we are committed.

NURSING/HEALTH CARE CENTER

Our Health Care Center is fully licensed by the State of Florida. Payment of the Admission Fee and Monthly Service Fee entitles each person to thirty days in-patient nursing care in the Health Care Center during any calendar year without additional daily rate charge; additional time is at a discount.

> Payment for hospitalization, ambulance, physician, therapists, dentists, opticians, podiatrists, private duty nurses, companions, medications, treatments, beauticians, barbers, personal laundry and other services and supplies and materials not ordinarily included in residential or nursing care must be paid separately and directly by the Resident.

If a Resident becomes so ill or disabled as to require continuing care in the Health Care Center, the Resident may continue occupancy as a Patient in the Health Care Center and the Village residential unit may be released.

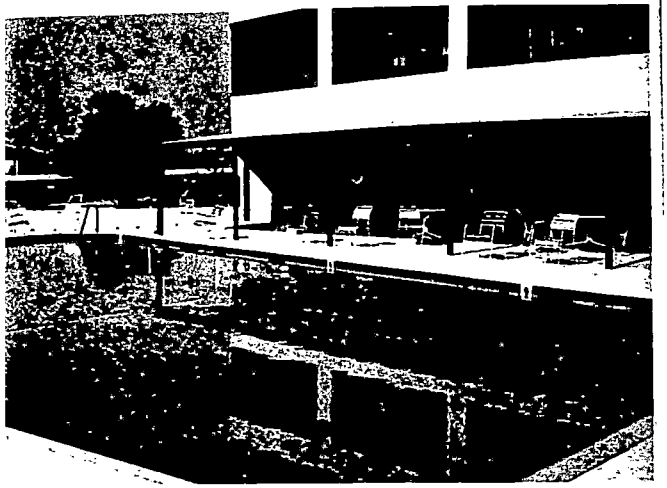
When one of a couple is permanently assigned to the Health Care Center, the one remaining in the residential unit pays the residential monthly charge for single occupancy for that unit with an option to move to a smaller unit if available.

WAITING LIST RESERVATIONS

Applicants who want to be placed on a waiting list to enter St. Mark Village in the future may do so by depositing $1,000 for a studio or one bedroom unit and $2,000 for a two bedroom unit. Priority will be given in accordance with the date of receipt of the Reservation Form and deposit.



c view from one of the casual lounge areas.



ol and deck area are easily accessible.



OWNERSHIP AND MANAGEMENT

While St. Mark Village is affiliated with Saint Mark Evangelical Lutheran Church, Dunedin, Florida, Inc.; St. Mark Village, Inc. directly operates and has the sole financial and legal responsibility for St. Mark Village and for the premises and obligations to Residents under their contract. Saint Mark Evangelical Lutheran Church, Dunedin, Florida, Inc., has no financial or legal liability for the operation of St. Mark Village or for the promises and obligations to Residents. St. Mark Village, Inc. has received a determination from the Internal Revenue Service of the United States Treasury Department that it is exempt from the payment of federal income tax under Section 501(c)(3) of the Internal Revenue Code.

This facility and all other continuing care facilities in the state of Florida are regulated by Chapter 651, Florida Statutes. A copy of the law is on file in this facility. The law gives you or your legal representative the right to inspect our most recent financial statement and inspection report before signing the agreement.

A Board of Directors, consisting of local Christian business and professional persons meet regularly to review the operation and set policy. They select the Executive Director and Nursing Home Administrator to manage the facility.

For an appointment and/or additional information, contact the St. Mark Village Office, (813) 785-2576, extension 712.

RATE SCHEDULE

Apartment Type	Admission Fees Effective: 5/1/85	Monthly Service Fees Effective: 1/1/88 Single	Double
Effective Date 1/1/89			
Studio	$29,500	$ 600	N/A
One Bedroom	$44,500	$ 765	$ 975
Two Bedroom	$59,000	$1010	$1220
Two Bedroom Deluxe	$67,000	$1145	$1355

Prices Subject to Change Without Notice.

St. Mark Village

2655 Nebraska Ave. (S.R. 584-A), just east of U.S. 19
Palm Harbor, Florida 34684, Ph. 813/785-2576



Bright, de
Gardens t



Friends.



MICHAEL BILIRAKIS
8TH DISTRICT, FLORIDA

COMMITTEE ON ENERGY AND COMMERCE
ENERGY AND POWER
HEALTH AND THE ENVIRONMENT
OVERSIGHT AND INVESTIGATION

COMMITTEE ON VETERANS' AFFAIRS
HOSPITALS AND HEALTH CARE
COMPENSATION, PENSION AND INSURANCE

CHAIRMAN, TASK FORCE ON
THE ELDERLY
CONGRESSIONAL HUMAN RIGHTS CAUCUS
ENVIRONMENTAL AND ENERGY STUDY
CONFERENCE
TRAVEL AND TOURISM CAUCUS
TASK FORCE ON CRIME

Congress of the United States
House of Representatives
Washington, DC 20515-0909

PLEASE RESPOND TO:

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1630 LONGWORTH HOUSE OFFICE BUILDING
WASHINGTON, DC 20515-0908
(202) 225-5755

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1100 CLEVELAND STREET, SUITE 1800
CLEARWATER, FL 34615
(813) 441-3721

☐ 2739 U.S. HWY. 19, SUITE 110
HOLIDAY, FL 34691
(813) 847-1022

☐ 408 WEST RENFRO STREET
SUITE 107F
PLANT CITY, FL 33566
(813) 752-9280

DATE 4/24/89 TIME _____

Total number of pages including the cover page: 10 pages

Please deliver to

Name: Rhett (Speechwriting)

Telephone/Telecopier number: _____

From

Name: Bob Meyers (Cong. Bilirakis)

Telephone/Telecopier number: 225-5755

Comments

ATTACHED is ① original memo to ADVANCE ② info on Cong. Bilirakis + Alzheimer's Disease

1 of 9

4/21 Brett - This has changed as to format - primarily due to time limits - now - it looks like only 20 minutes or so @ the facility

Bob Meyers

MEMORANDUM

TO: White House Advance

FROM: Bob Meyers (Rep. Bilirakis)
225-5755 (w) 703-549-0132 (h)

RE: President's visit to St. Mark Village, Palm Harbor, Florida

DATE: 4/21/89

Purpose of Visit:

The President will be visiting Palm Harbor to participate in a ceremony to dedicate the "Michael Bilirakis Alzheimer's Center". The center contains nursing and "assisted living" quarters specifically designed for the care of Alzheimer's Disease patients.

The center was named after Congressman Bilirakis to recognize his long interest and legislative activity with regard to Alzheimer's Disease. The Congressman introduced successful legislation to provide for Medicare demonstration projects for Alzheimer's Disease as well as family support groups.

The Michael Bilirakis Alzheimer's Center is located at St. Mark Village, a congregate living facility. At present, the center contains 20 nursing beds and 31 assisted living apartments for those afflicted with Alzheimers. Altogether, St. Mark Village contains 324 living units and approximately 500 residents. St. Mark Village is a not-for-profit independent corporation founded by the St. Mark Lutheran Church of Dunedin, Florida.

Outline of the Event:

A proposed timeline for the President's visit is attached. In general, it is contemplated that there will be a ceremony on stage at which the President will make some brief remarks commenting on: (a) Congressman Bilirakis and his work in the area of Alzheimer's Disease and (b) the President's concern for adequate health care for the elderly -- especially with regard to debilitating diseases like Alzheimers.

(722)
700
Gilbert
$1400

2479

I have attached separate talking points on both (a) and (b). More broadly on these points -- we feel the dedication presents a good opportunity for the President to draw national attention to Alzheimer's Disease and health care for the elderly. Nearly 500 elderly people live at St. Mark Village -- and the new center is one of the few in the country specifically designed for A.D. Therefore, the "backdrop" is excellent for any remarks or message of this kind.

Participants on Stage:

At present, only the following people are contemplated to be on stage with the President:

(1) Congressman Bilirakis, his wife, Evelyn and their son, Gus.

(2) Ed Hutfliz, Executive Director of St. Mark and his wife.

(3) Pastor Fresh, President of the Board, St. Mark Village and his wife.

(4) Governor Martinez (possible)

(5) Representative Bill Young (possible)

(6) Senator Connie Mack and Senator Bob Graham (invited)

Audience:

The size of the audience will depend on the determination of the White House advance team as to whether the St. Mark courtyard is a suitable location -- or whether the event must be held in the auditorium. The auditorium seats approximately 300 people. The courtyard will accomondate several hundred to over 1,000 people.

In any event -- the composition of the audience will be: (a) residents of St. Mark Village who are physically able to attend (the event will be transmitted through television to those who are "room bound." (b) local Republican officials, committemen, supporters of President Bush and Congressman Bilirakis, (c) local senior group members and officials included NARFE and AARP.

As a gauge to crowd size -- town meetings which Congressman Bilirakis has held in this area have exceeded 800 people. The surrounding area is filled with large retirement communities and apartment complexes. Given the publicity the event will receive, the natural expectation would be for a large turnout.

3 of 9

Reception:

A reception for approximately 100 people is also planned for the event. Participants at this event would primarily be: St. Mark Board of Directors, local officials and close supporters of Congressman Bilirakis. Planning would include opportunity for photographs.

Media:

In addition to media traveling with the President, the expressed interest of the local television, radio and newspapers is exceedingly high. President Bush is very popular in Pinellas County (which maintains the highest number of Republican registrants in the state). To the extent possible, we would want to provide access for our local press.

Plauqes -- President:

As part of the dedication ceremony, we would like to request that the President present a plaque to Congressman Bilirakis and Pastor Fresh, Chairman of the Board, St. Mark Village. Under the proposed schedule, the plaques would be presented following the President's remarks.

President's Remarks:

Two memos have been attached which outline (a) Congressman Bilirakis' work on Alzheimer's Disease and (b) the disease generally.

As you may know, Alzheimer's Disease extracts a heavy toll from both the patient -- who gradually becomes disoriented and incapable of caring for him or herself -- and the family which seeks to care for the patient and has the exceedingly stressful experience of watching a loved one undergo this transformation.

Therefore, if there is any one overriding theme to this event, it is one of compassion and caring. Right now, there is no cure for Alzheimer's Disease although research is ongoing. Therefore, the primary challenge is one of care for the patient and support for the family.

Alzheimer's is a terrifying disease which extracts a heavy toll from society. The President's remarks should reflect this somber fact.

499

CONGRESSMAN BILIRAKIS' WORK ON ALZHEIMERS DISEASE

Florida's Ninth District has one of the highest concentrations of elderly citizens in the country, thus the prevalence of Alzheimer's Disease is very high there as it is a disease which afflicts individuals in the mid to late-life years.

* Congressman Bilirakis always has been active legislatively regarding Alzheimer's Disease.

98th Congress:

* Introduced a bill directing HHS to set up a network of family support groups in universities and other facilities that were receiving federal funds for Alzheimer's research. These support groups would help victims in the early stages of Alzheimer's Disease. They would also help the family members to cope with the ravages of Alzheimer's Disease on their loved one.

* Introduced a bill calling for the establishment of 10 one-year demonstration projects to determine the feasibility of providing Medicare assistance for Alzheimer's Disease. Alzheimer's Disease often can take as long as 20 years to run its course, thus the financial implications for a family with an Alzheimer's patient can be devastating.

99th Congress:

* As Florida's only member on the Energy and Commerce Committee's Health and Environment Subcommittee, he steered both bills through the Congress to passage into law. The first bill was passed as an amendment to the Protection and Advocacy Services for the Mentally Ill Persons Act of 1986. The demonstration projects also were passed and became Public Law 99-509.

While Congressman Bilirakis proposed 10 one-year projects, the law calls for the establishment of five three-year demonstration projects. HHS is in the process of beginning these projects.

Current:

* Congressman Bilirakis annually cosponsors legislation designating November of each year as "Alzheimer's Disease Awareness Month."

* Congressman Bilirakis always lends his assistance to local Alzheimer's Disease projects. He has assisted the Alzheimer's Disease Support Groups and aided the Pasco County Sheriff's Department in its goal of providing identification bracelets for Alzheimer's Disease patients. He has visited institutionalized patients who are stricken with Alzheimer's Disease.

* In recognition of his efforts for Alzheimer's Disease patients and their families, St. Mark's Village has chosen to honor him by naming its new facility the Mike Bilirakis Alzheimer's Wing.

# # # # #

599

TALKING POINTS ON ALZHEIMERS DISEASE

Background:

*** Alzheimer's Disease was discovered in 1906 by Alois Alzheimer, a German neurologist. It is a progressive disease of the brain affecting memory, thought processing and language. It is the fourth leading cause of death in the elderly. There is no cure.**

More than four million persons are now affected by Alzheimers Disease. By the year 2000, it is projected that 7.4 million people will be affected by the disease. At that time, as much as a quarter of the U.S. population will be over 50 and will be at some risk of being stricken by the disease. About one of eight will be 65 or older and at heightened risk.

With the increase in the elderly population, we will get a corresponding increase in the number of people who will be afflicted by the disease unless a cure is found.

* Victims of the disease are individuals of either sex who are usually beyond their mid-life years. Alzheimers may often take as long as 20 years to run its course.

Changes occur gradually in the brain cells and at first symptoms are barely noticeable. As the disease progresses, memory loss progresses to a significant degree and there are other changes in behavior that can result in lead an individual degenerating into a vegetative state.

* When an Alzheimer's victim dies, the disease isn't normally listed on the death certificate as a cause of death because persons don't die from brain cells not functioning. However, persons in vegetative states (as a result of Alzheimer's Disease) can develop serious infection resulting in death.

Possible Causes Of Alzheimer's:

1.) Genetic Factors -- includes familial (a pattern in a family suggesting the disease is inherited) aggregation, association with Down's syndrome, and altered DNA-binding proteins.

2.) Exaggerated Aging -- symptoms of the disease such as senility and dementia, are not part of the normal aging process.

3.) Environmental Factors -- includes metal exposures, head trauma, viruses and other infectious agents.

4.) Immunologic Factors -- includes special susceptibility to infectious agents reacting with one's own brain cells.

5.) Disrupted nerve cell circuits -- includes loss of specific populations of nerve cells and disruption of communication between certain groups of brain cells.

6.) Intrinsic Metabolic Factors -- includes disruption of biochemical pathways in brain cells.

6 of 9

Financial Impact On Families:

Devastating, primarly because Alzheimers patients aren't covered under the Medicare program. Approximately $80 million is spent annually on the cost of care for Alzheimers Disease.

Treatment:

Virtually non-existent. FDA is conducting clinical trials across the nation on THA, a drug that allegedly depresses enzymes that destroy the brain transmitter, which has deteriorated as a result of the disease. The brain transmitter allows cells to communicate with each other. While preliminary studies have conflicting results about the effects of THA, FDA is still funding clinical trials on THA. Currently, 300-400 people are participating in these trials.

Government Funding:

Research only. Congress approved an increase in federal funds being spent on Alzheimer's Disease research to $120 million in FY89. This is a 32% increase over FY88, but amounts to just $30 per patient.

# # # # #

7 of 9

Mike Bilirakis was first elected to Congress on November 2, 1982, defeating Democrat George Sheldon in a closely contested race.

In 1984 and 1986, however, Mike Bilirakis soundly defeated his Democratic challengers, drawing broad support from all areas of the Ninth Congressional District -- a district that spans northern Pinellas, Pasco and parts of Hillsborough Counties.

Mike was born in the Ninth District, in Tarpon Springs, on July 16, 1930. Shortly after his birth, however, Mike's Greek immigrant parents, Emmanuael and Irene, left the area for Pennsylvania.

Early in life, Mike developed a "work hard and work your way up philosophy". He experienced poverty as a young man, but he always had a clear vision of a better future. He knew that to "play with the cards he had been dealt" he would not be able to provide for his family in the manner he desired. The only course available was to work his way up the ladder.

8 9 9

Growing up in Pittsburgh, then, Mike worked hard in the steel mills, saving money he would later need for college. He worked the night shift to pay his way to an engineering degree at the University of Pittsburgh and later, he also graduated from law school at the University of Florida.

After several varied jobs, including work on an oil rig in the Gulf of Mexico and with a local aerospace firm, Mike opened his own law practice in Holiday in 1969. He later invested in land and small businesses and taught several courses at local community colleges. In addition, Mike accepted appointments as county and municipal judge, traveling often to Dade City to preside over cases.

Today, Mike's diverse background and experience are paying off for residents of the Ninth Congressional District as he continues his work habits as a three-term incumbent. Mike is perhaps the only petroleum engineer in the U.S. Congress -- important to his work on the Energy and Commerce Committee.

9/9

As a veteran and member of the House Veterans Affairs Committee, Mike also has taken an active role in veterans legislation. His work helped to bring a new V.A. outpatient clinic to Pasco County, and and he has hosted several veteran committee meetings and workshops in the district. Mike has also taken a keen interest in the matter of American POWs and MIAs in Southeast Asia, having traveled to Vietnam and Laos in pursuit of new information on our missing veterans.

Mike's tough-minded philosophy is also paying off for his family as his two sons pursue advanced degrees. Currently, his son Manuel is studying medicine at the University of Miami while Gus is a law student at Stetson University in DeLand.

Along with his wife, Evelyn, Mike travels throughout the Ninth District at every opportunity. Fulfilling a campaign promise made long ago, Mike continuously visits local groups and listens to citizens, seeking always to be a "true representative of the people."

MICHAEL BILIRAKIS
9TH DISTRICT, FLORIDA

COMMITTEE ON ENERGY AND COMMERCE
ENERGY AND POWER
HEALTH AND THE ENVIRONMENT
OVERSIGHT AND INVESTIGATION

COMMITTEE ON VETERANS' AFFAIRS
HOSPITALS AND HEALTH CARE
COMPENSATION, PENSION AND INSURANCE

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THE ELDERLY
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CONFERENCE
TRAVEL AND TOURISM CAUCUS
TASK FORCE ON CRIME

Congress of the United States
House of Representatives
Washington, DC 20515-0909

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CLEARWATER, FL 34615
(813) 441-3721

☐ 2739 U.S. HWY. 19, SUITE 110
HOLIDAY, FL 34691
(813) 947-1022

☐ 408 WEST RENFRO STREET
SUITE 107F
PLANT CITY, FL 33566
(813) 752-9260

DATE 4/25/89 TIME 1:55

Total number of pages including the cover page: 3

Please deliver to

Name: Rhett (Speechwriting)

Telephone/Telecopier number: _____

From

Name: Bob Meyers (Rep. Bilirakis)

Telephone/Telecopier number: 225-5755

Comments

If you need anything else, just give me a call

Losing A MILLION MINDS — OTA - April 1987

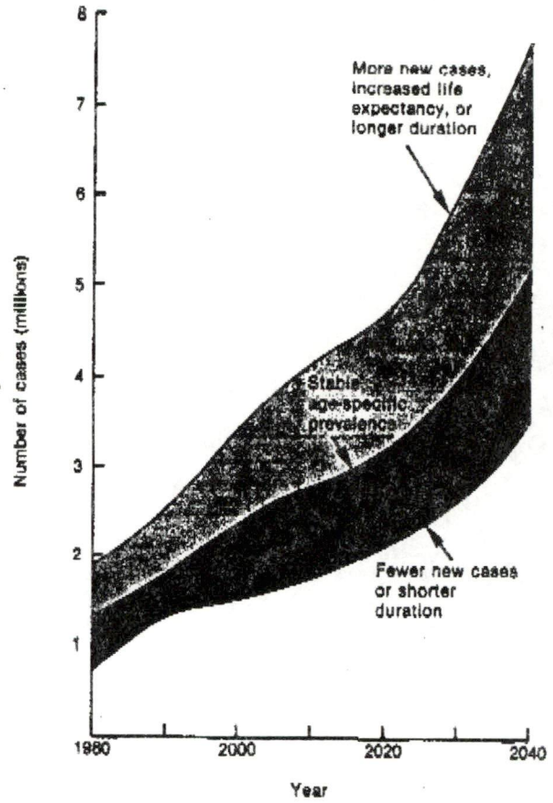
Chapter 1

Dementia: Prospects and Policies

Disorders causing dementia—the loss of mental functions in an alert and awake individual—will constitute a large and growing public health problem until well into the next century. Today, an estimated 1.5 million Americans suffer from severe dementia—that is, they are so incapacitated that others must care for them continually. An additional 1 million to 5 million have mild or moderate dementia (27). Ten times as many people are affected now as were at the turn of the century (79). The number of people with severe dementia is expected to increase 60 percent by the year 2000. Unless cures or means of prevention are found for the common causes of dementia, 7.4 million Americans will be affected by the year 2040—five times as many as today (see figure 1-1). The middle line on figure 1-1 assumes no change over time in the probability of developing severe dementia at a given age, and it does not hinge on new births but rather projects cases of dementia based on those already born. Further increases in life expectancy would increase the number of cases expected, and finding means to prevent dementing disorders would lower it.

The public has only recently become aware of the problems posed by dementing illnesses. Dementia and Alzheimer's disease (AD) have become household words only in the last few years. Efforts of national organizations, such as the Alzheimer's Disease and Related Disorders Association (ADRDA), have emphasized the plight of families and publicized the problems faced by nationally famous individuals who have developed dementia (e.g., Rita Hayworth). The most prevalent disorder causing dementia, Alzheimer's disease, has risen from relative obscurity to the cover of *Newsweek* magazine, the pages of *Life*, and prime-time television ("Do You Remember Love?" a made-for-television movie aired by CBS in May 1985). One book on caring for patients with dementia, *The 36-Hour Day* (74), has sold over 500,000 copies, and several other books for the general public have found sizable audiences (21, 48,84).

Figure 1-1.—Current and Projected Cases of Severe Dementia in the United States, 1980-2040



SOURCE: P.S. Cross and G.J. Gurland, "The Epidemiology of Dementing Disorders," contract report prepared for the Office of Technology Assessment, 1986.

Interest among health and social service professionals has risen in parallel with public awareness. Medical attention to Alzheimer's disease began to increase in the 1970s, catalyzed in 1976 by an editorial in a medical journal calling attention to the high prevalence and perniciousness of the disease (61) and by activities supported by various Federal research institutes (the National Institute on Aging, the National Institute on Neurological and Communicative Disorders and Stroke, and the National Institute of Mental Health). Dozens of professional books, special is-

ALZHEIMER'S ASSOCIATION
Someone to Stand By You.

STATISTICS ON ALZHEIMER'S DISEASE

Alzheimer's Disease (AD) is a progressive, degenerative disease that attacks the brain and results in impaired memory, thinking, and behavior. It is the most common form of dementing illness. The person with AD may experience confusion, personality and behavior changes, impaired judgment, and difficulty finding words, finishing thoughts or following directions.

The following estimates were compiled by the Alzheimer's Association:

- More than 4 million people are afflicted with AD.
- AD is the fourth leading cause of death among adults, taking more than 100,000 lives annually.
- Approximately 70-80 percent of AD care is provided by families. The cost to a family caring for the AD patient averages $22,000 annually.
- Over 60 percent of all nursing home patients are victims of AD or a related disorder. Average cost for nursing home care is estimated at $25,000 per year.
- AD costs the country over $80 billion annually. The federal government covers $4.4 billion and the states, another $4.1 billion. Much of the remaining costs are borne by patients and their families.
- More than 11 percent of the population over 65 is afflicted with AD and the percentage rises to 25-50 percent of those over age 85. The life span of Alzheimer victims can range anywhere from 3 to 20 or more years.
- A projected 7.4 million Americans will have a severe form of AD or a related disorder by the year 2040 if no cure or treatment is found.
- Congress approved an increase in federal dollars being spent on AD research to $120 million in fiscal year 1989. This figure represents a 32 percent increase in research funding over the previous year, but amounts to only $30 per patient.

ALZHEIMER'S DISEASE AND RELATED DISORDERS ASSOC. INC.
70 E. Lake Street, Suite 600 · Chicago, Illinois 60601 · Phone: (312) 853-3060

drug abuse and all it's related problems; hospital work (I have always worked in hospitals); crime in the streets; and on and on. It suddenly became obvious to me that I should get interested in none of these projects. That I should throw all my energies into helping wipe out illiteracy. Every single thing that worries me would be helped if more people could read.

For instance, there are 8 million Americans who are unemployed and yet The Wall Street Journal tells us that employers can't find enough applicants who are sufficiently skilled in basic reading, writing, and math to fill the empty positions. Also, there is a direct correlation between crime and illiteracy. The California Youth Authority says that 50% of their inmates are functional illiterates, that is, reading below the 6th grade level. Florida Judge Charles Philips reports that "80% of new criminals who pass my desk would not be here if they had graduated from high school and could read and write." I could go on and on, but this is a little like telling Noah about the flood!!!!

George didn't become President, but it turns out that Vice Presidents' wives can also raise a crowd. So I am spending my time visiting schools, libraries, churches, service groups, clinics, colleges, and community centers encouraging reading, the teaching of reading, the necessity of reading, and the joys of reading. I am also encouraging the giving of time and money from individuals and corporations toward the fight against illiteracy.

As always is the case, I have gained much more that I have given. I have seen a legally blind man, Jack Gordon in Boston, teach two children to read. He says "How do I know? I can't see. Now you spell it and sound it out". They do and the joy they get and he gets is so thrilling.

I have seen a school in Philadelphia, run by a tiny staff of 3 nuns and parents. Many of these parents are on welfare, but they know the importance of an education and rush twice a month with their $25 to pay the tuition. They know that an education is the key that unlocks the door to the American Dream and that no sacrifice is too big.

I have seen the parents in The Briargrove Elementary School in Houston, the exact other end of the spectrum, being teachers aides and so thrilled with the dramatic rise in the test results. Thank heavens we are bonding parents and schools again.

I have seen a kindergarten teacher at the Webb School in The District teach 5 year olds to read. Watching her teach was like watching an athletic event. The energy Ann Derricote put into her teaching was an inspiration.

In Boston alone they have 3000 volunteers in 50 schools and could use twice that many. It was there I saw a wonderful stylish lady teaching French as a volunteer. She was pulling the most amazing things out of her pocketbook, and the children and she were saying the words in French and English. I was told that she has done this for years and is a very effective teacher.

I wonder if you know that Adele Rogers, the wife of former Secretary of State, William Rogers, has tutored 2 days a week for the past 10 to 15 years: 1 morning in the N.Y.C. public school system and 1 morning a week in the D.C. school system. We all know that Governor James Hunt of North Carolina and his wife volunteer in the public school system 1 morning a week.

This is just a small representation of the wonderful people I have seen.

Many corporations are helping. They are permitting their employees to give several hours a week on company time. I visited with one lady who was on loan from Prudential. She said that the wonderful thing about the program was that now she knew how to help her own children at home.

In New York City where 15,000 volunteers help in 544 schools I met with a group helping Cambodian children learn English and learn to read. One rather aged lady told me that she had been desperately lonely until she volunteered and her eyes filled with tears in the remembering. Then her face lit up as she told me that "she had never been lonely a day since".

I have visited schools in Baltimore, NYC, Houston, Philadelphia, Milwaukee, The District of Columbia, and San Antonio, Texas. I have been very impressed with the volunteerism from every sector. But even more than that I have been so impressed with the superintendents, principals, teachers, and librarians. I am impressed with the dedication of these wonderful people who work in hot crowded classrooms for less material satisfaction than most, doing their own jobs and sometimes ours.

I have also learned that one person can make a difference. Just look at the job Margaret McNamara did! She started--one woman--in one D.C. public school, and today there are over 100,000 volunteers in the Reading Is Fundamental program and nearly 40% of them are parents. What a joy these book distributions have been for me. Someone else, usually many someone elses, do a lot of work selecting books, setting up programs, and arranging the day. I come in on the big day to help distribute the books. Wonderful!!! Right here in the Steven's School we met Sandra Speier, an extraordinary Reading Specialist. Her second grade class was told a very scarey Halloween Story by twins of the same age before the book distribution. For me, the icing on the cake!!!!

Just last Thursday in San Antonio I went to the Smith Elementary School for a RIF distribution. There the students sang a great song written by their Resident Poet. The chorus was "I need to read, I really need to read." I wish you could have seen those precious children carefully choosing their very own books!!!

Look at Marty Van Arsdale in upper N.Y. She read about "Project Read," a program started in Idaho, and started this same simple project in Wyoming County, N.Y. She worked through every known group--schools, libraries, churches, men's clubs, community centers--just every group who would listen. She flooded the county with bumper stickers and posters and word of mouth saying, "Have you read to your child 15 minutes today?" She got the children and teachers on her side and they worked on their parents. They found the reading interest way up and as an added bonus, the time spent side-by-side nested by their child did wonders for family relationships. One lady had an idea!!!

I couldn't be in this great library without mentioning my trips to two other great libraries, The Enoch Pratt Library in Baltimore, and The New York City Public Library. Both these wonderful institutions do a great job in adult illiteracy. Their programs have helped people do such things as enter a high school equivalency program, obtain a job, get a driver's license, do such heart-warming tasks as read out loud bedtime stories to their own children, read the Bible, and write letters to their friends and loved ones. Tasks they had never been able to do before!!

I read with great interest the three purposes of this symposium. I am not qualified to recommend priorities in national educational policy relating to reading. I am not qualified to help the four sponsoring organizations shape their goals and programs for the immediate future. But as an enthusiastic cheerleader I can help focus national attention on the essential role of an active, two way family-school partnership in encouraging reading. I am more than willing to help. Please call on me when you need me.

The job is immense and when I get discouraged by the enormity of 23 million known illiterates in this country, I remember that magnificent Helen Keller who said that "Literature kept her from being disenfranchised from life." Deaf and blind Helen Keller could read!!!

Somebody taught Helen Keller to read!!!!

While she was there, one older lady told Bar how desperately lonely she had been until she volunteered. Her eyes filled with tears in the remembering. And then her face lit up, as she told Barbara, "I have never been lonely a day since."

One need matches another need -- and a wonderful thing happens. You come up with an answer that money just can't buy. That's one reason we need to rely less on the collective wallet, and more on collective will.

The society that worships money -- or sees money as a cure for all that ails it -- is a society in peril. But we are not that kind of people. And we must do more than wish we had more to spend. Because the challenge of education reform suggests something much more fundamental than money.

Already, we spend more on education than on defense. We spend more money per student per year than any other country in the world -- including Japan. Federal spending for education -- which is only a fraction of the total -- has increased 66 percent over the last decade.

One thing I learned in school is sometimes there's more than one right answer. More spending -- that isn't the only right answer, or even the best answer. What is needed -- what this conference is all about -- is a shared determination on the part

We're expanding on a Good Idea!

St. Mark Village

The Total Care Ministry of
St. Mark Lutheran Church
"Open to All Faiths"

2655 Nebraska Ave. (S.R. 584-A)
Palm Harbor, Florida 34684

Your Home with a Heart
...at the Heart of Pinellas

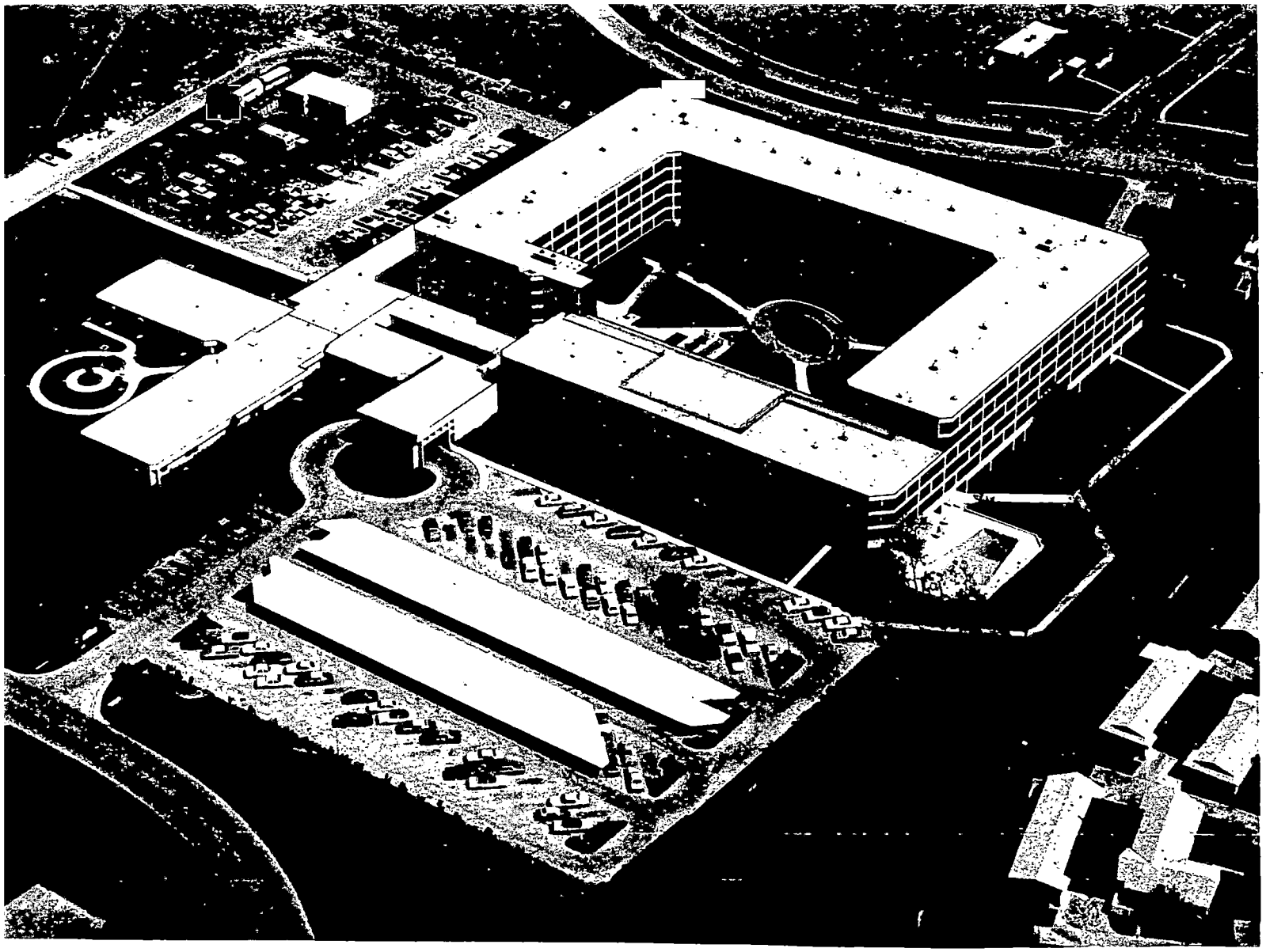
This unique retirement community is ideally located... in Palm Harbor, close to parks, beaches, golf courses, lakes and all the other advantages of highly-sought Pinellas County. The Village is only steps from supermarkets, drug stores and banks with Transit Authority buses at our corner and our own minibus for residents' use.

So the Village is not only an enormously enjoyable way to live, it's a wonderfully convenient place to live.

Come Join Us!

You are invited to share the freedom, fellowship and round-the-clock care enjoyed by the St. Mark Village family. Here clearly, is peace-of-mind for your ultimate years. Ask the Village office for application forms.

St. Mark Village
2655 Nebraska Ave. (S.R. 584-A), just east of U.S. 19
Palm Harbor, Florida 34684, Ph. 813/785-2576



11.5 Acres of Amenities for your Luxurious Living... with safety, security and Round-the-Clock Christian Care

St. Mark Village is the fulfillment of dreams — yours and ours.

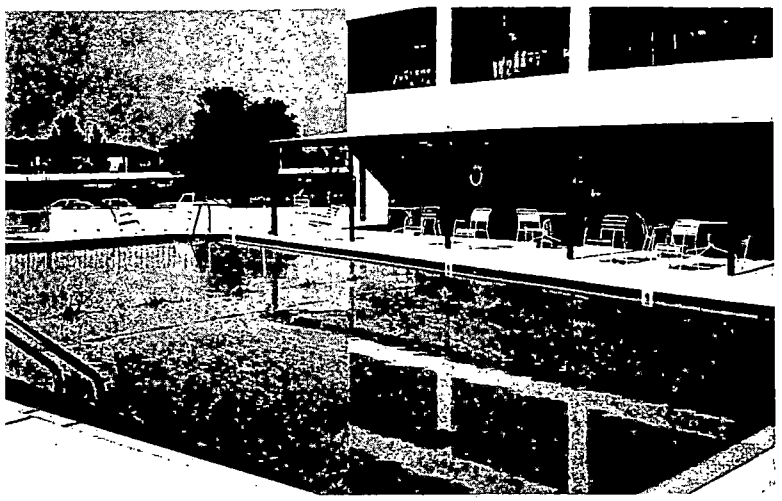
Your dream: to enjoy the rest of your life as the best of your life — with assurance your physical, social and spiritual needs will be answered. Our dream: to create a non-profit Christian retirement community providing this assurance in full.

The Village contains 324 deluxe studio, one bedroom and two bedroom apartments, each with a complete kitchen. Community facilities include the beautiful dining room (table service), spacious chapel, lovely lounges (and additional lounges on each floor), hobby and craft rooms, library, game rooms, heated swimming pool and whirlpool, shuffleboard, landscaped grounds.

The 60-bed Health Care Center provides ever-present professional attention. Thirty days care in the center is available to each resident per year without additional daily rate charge; additional time is at a discount. All Village apartments have direct emergency communication with the nursing center.



A panoramic view from one of the casual lounge areas.



An ample pool and deck area are easily accessible.



Your own private balcony.

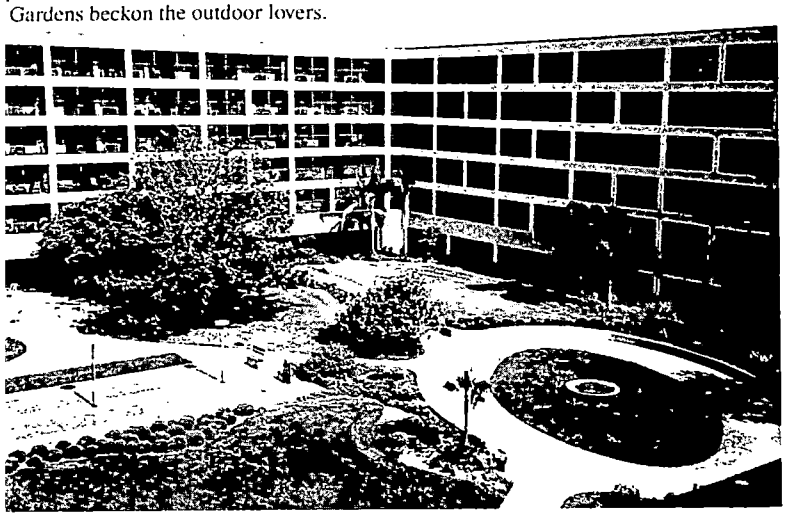
Enjoy these outstanding benefits and features at St. Mark Village

- Full meal daily served in dining room
- Weekly maid service
- All utilities furnished even local phone calls
- Soundproof and fireproof construction
- Complete all-electric kitchen including disposal
- Private balcony
- Individual heat and air-conditioning controls
- Carpeting and draperies
- Walk-in closets
- Luxurious lobby and lounges: laundry, storage rooms and lounges on each floor
- 3 resident elevators
- Reserved parking place
- Emergency nurse-call system
- Smoke and heat detectors
- Auxiliary power generator
- Security patrol
- Swimming pool
- Hi-temperature whirlpool
- Shuffleboard
- Men's Den with pool table
- Card and game rooms, library
- Craft, hobby and woodworking shops
- Social director
- Deluxe 60-bed nursing home
- 30 days in nursing center per person per year
- Day and night medical service and nursing staff
- Physical and rehabilitative therapy
- Dietician



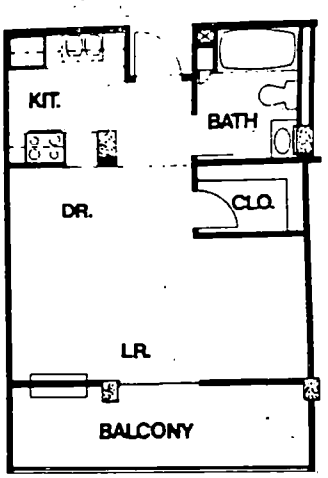
Bright, delightful dining room.

Gardens beckon the outdoor lovers.

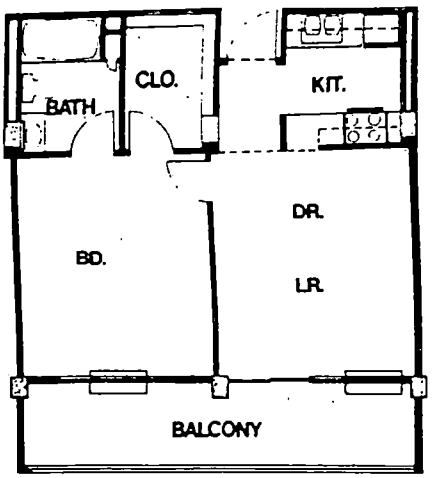


Friends, fellowship, food and fun.



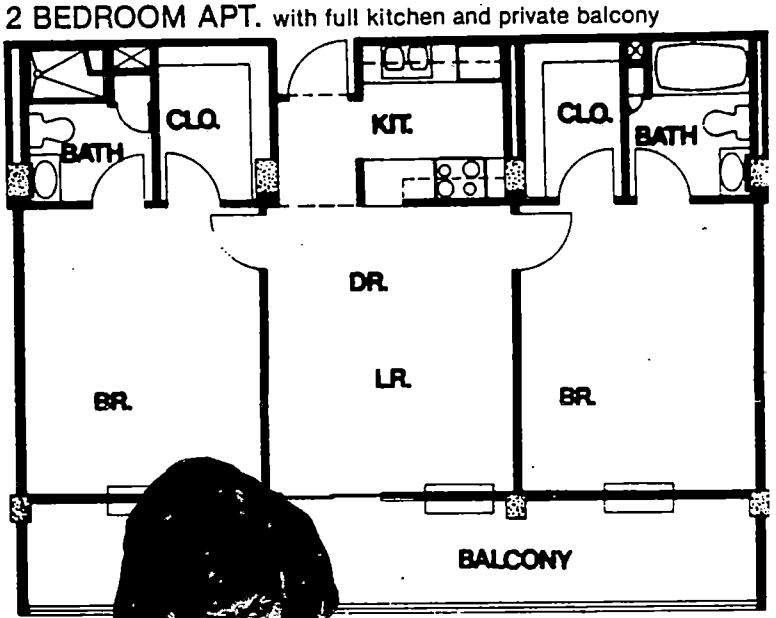


STUDIO APT.
with full kitchen
and private balcony



1 BEDROOM APT.
with full kitchen
and private balcony

2 BEDROOM APT. with full kitchen and private balcony



Complete range of conveniences.



St. Mark Village

YEURITH WAY
SALES COUNSELOR

St. Mark Village
P.O. Box 1449, Palm Harbor, FL 34682-1449
2655 Nebraska Ave., Palm Harbor, FL 34684
Telephone (813) 785-2577, Ext. 712

Enjoy these outstanding benefits and features at St. Mark Village

- Full meal daily served in dining room
- Weekly maid service
- All utilities furnished even local phone calls
- Soundproof and fireproof construction
- Complete all-electric kitchen including disposal
- Private balcony
- Individual heat and air-conditioning controls
- Carpeting and draperies
- Walk-in closets
- Luxurious lobby and lounges: laundry, storage rooms and lounges on each floor
- 3 resident elevators
- Reserved parking place
- Emergency nurse-call system
- Smoke and heat detectors
- Auxiliary power generator
- Security patrol
- Swimming pool
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- Shuffleboard
- Men's Den with pool table
- Card and game rooms, library
- Craft, hobby and woodworking shops
- Social director
- Deluxe 60-bed nursing home
- 30 days in nursing center per person per year
- Day and night medical service and nursing staff
- Physical and rehabilitative therapy
- Dietician

"We're expanding on a Good Idea!"

St. Mark Village is a non-profit retirement community and health care center (nursing home) sponsored by St. Mark Lutheran Church, Dunedin, Florida, but entirely self-supported financially. Our mission is to provide superior living facilities as free of cares as it is possible for us to make them in an environment of Christian love and concern.

QUALIFICATIONS FOR RESIDENCY

St. Mark Village welcomes applications for Residents from active retired or semi-retired people who: (1) Seek deluxe apartment living free of maintenance and housekeeping drudgery with the security of around-the-clock communications with health care professionals; (2) Are 62 or more years of age, are ambulatory, able to live alone without assistance and are in reasonably good physical and mental health (when double occupancy is involved each person must meet these standards); (3) Are of good moral character; (4) Are financially able to meet the charges related to the accommodations occupied as well as their supplementary personal needs.

RESIDENTIAL FACILITIES AND SERVICES

Payment of the Admission Fee and the regular residential Monthly Service Fee provides a residential unit with kitchen, wall-to-wall carpeting, drapes, screened balcony, weekly maid service, maintenance, utilities including heat, air conditioning and local telephone calls, central TV antenna connection, one meal per day served in the dining room and scheduled minibus service.

Spiritual, social and recreational activities are available. Lobbies, lounges, public balconies and patios, an ice cream parlor, a beauty shop, conference room, chapel, arts and crafts room, and game room are all available for your use and enjoyment. Private dining rooms are available for special occasions at a nominal fee. Outdoor facilities in the landscaped grounds include shuffleboard courts, a swimming pool and high temperature whirlpool spa. You will be assigned your own parking space for your car.

Your own private balcony.

'he Health Care Center is available for certain ut-patient services at a nominal charge as well as ı-patient care. Nursing services are available for mergency assistance 24 hours a day. Emergency ignalling from your bedroom and bathroom are vailable if you are unable to telephone for ssistance. If you don't make routine appearances uch as for meals, we will check to learn if you are /ell.

APPLICATION FOR ADMISSION

Vhen you have selected the unit you prefer, you will e given application forms which include: l) Deposit — your application must include a eposit of 10% of the Admission Fee. If your pplication is not approved, this deposit will be efunded in full. Checks for deposit toward the \dmission Fee should be made payable to the First Jational Bank of Clearwater, Trustee for St. Mark /illage, Inc., (2) Minister's statement — a letter of haracter reference must be completed by your astor and returned by him directly to St. Mark /illage. (3) Personal information — personal and inancial information is kept in strict confidence. The Minister's Statement and Personal Information orms should be returned to us as soon as possible or consideration by the Acceptance Committee. (4) Processing — completed applications usually an be processed within 2 weeks or less after we eceive them. You will be advised immediately of he action of our Admissions Committee.

ADMISSION FEE

Ten percent of the Admission Fee is required at the ime of your initial application. The balance will be lue thirty days after notice to you that the residential nit will be ready for occupancy, or upon your aking occupancy, whichever comes first. If you withdraw your application after approval, but before occupancy, the Admission Fee or portion of the Fee ou have paid will be refunded less a processing fee of 4% of the full Admission Fee.

Our refund policy provides a "trial period" of four ears. If you decide to leave St. Mark Village during hat time, the Admission Fee will be refunded less a 4% processing fee and less 2% per month for each nonth or fraction of a month you have lived here.

MONTHLY SERVICE FEE

The Monthly Service Fee is billed in advance and payable monthly on the date of occupancy or thirty days after notice to you that the residential unit is ready for occupancy, whichever occurs first. If you are away from St. Mark Village for thirty consecutive days or more, an absentee credit will be allowed against the monthly service fee (based on reduced food service only).

Although subject to adjustment, the Monthly Fees will be maintained at the lowest possible rate consistent with sound financial practices and maintenance of the quality and services to which we are committed.

NURSING/HEALTH CARE CENTER

Our Health Care Center is fully licensed by the State of Florida. Payment of the Admission Fee and Monthly Service Fee entitles each person to thirty days in-patient nursing care in the Health Care Center during any calendar year without additional daily rate charge; additional time is at a discount.

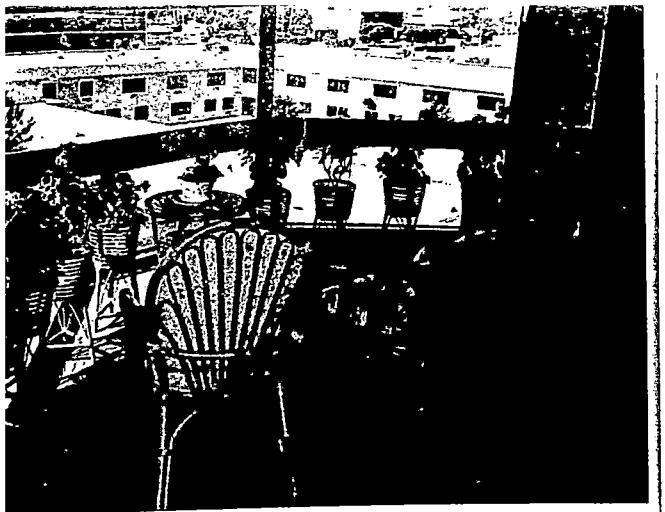
> Payment for hospitalization, ambulance, physician, therapists, dentists, opticians, podiatrists, private duty nurses, companions, medications, treatments, beauticians, barbers, personal laundry and other services and supplies and materials not ordinarily included in residential or nursing care must be paid separately and directly by the Resident.

If a Resident becomes so ill or disabled as to require continuing care in the Health Care Center, the Resident may continue occupancy as a Patient in the Health Care Center and the Village residential unit may be released.

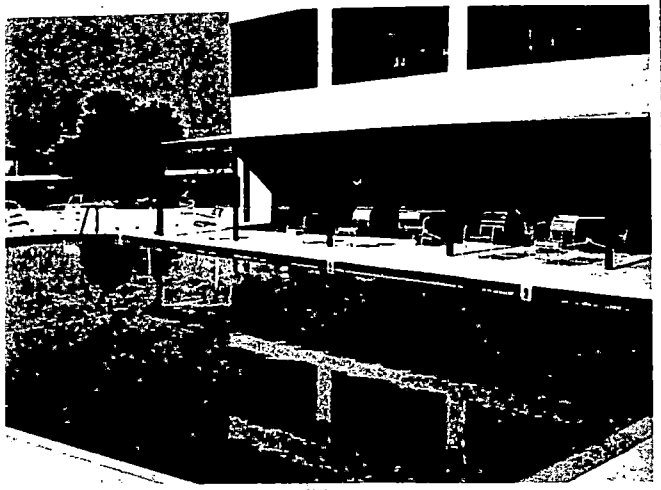
When one of a couple is permanently assigned to the Health Care Center, the one remaining in the residential unit pays the residential monthly charge for single occupancy for that unit with an option to move to a smaller unit if available.

WAITING LIST RESERVATIONS

Applicants who want to be placed on a waiting list to enter St. Mark Village in the future may do so by depositing $1,000 for a studio or one bedroom unit and $2,000 for a two bedroom unit. Priority will be given in accordance with the date of receipt of the Reservation Form and deposit.



c view from one of the casual lounge areas.



ol and deck area are easily accessible.



OWNERSHIP AND MANAGEMENT

While St. Mark Village is affiliated with Saint Mark Evangelical Lutheran Church, Dunedin, Florida, Inc.; St. Mark Village, Inc. directly operates and has the sole financial and legal responsibility for St. Mark Village and for the premises and obligations to Residents under their contract. Saint Mark Evangelical Lutheran Church, Dunedin, Florida, Inc., has no financial or legal liability for the operation of St. Mark Village or for the promises and obligations to Residents. St. Mark Village, Inc. has received a determination from the Internal Revenue Service of the United States Treasury Department that it is exempt from the payment of federal income tax under Section 501(c)(3) of the Internal Revenue Code.

This facility and all other continuing care facilities in the state of Florida are regulated by Chapter 651, Florida Statutes. A copy of the law is on file in this facility. The law gives you or your legal representative the right to inspect our most recent financial statement and inspection report before signing the agreement.

A Board of Directors, consisting of local Christian business and professional persons meet regularly to review the operation and set policy. They select the Executive Director and Nursing Home Administrator to manage the facility.

For an appointment and/or additional information, contact the St. Mark Village Office, (813) 785-2576, extension 712.

RATE SCHEDULE

Apartment Type	Admission Fees Effective: 5/1/85	Monthly Service Fees Effective: 1/1/88 Single	Double
Effective Date 1/1/89			
Studio	$29,500	$ 600	N/A
One Bedroom	$44,500	$ 765	$ 975
Two Bedroom	$59,000	$1010	$1220
Two Bedroom Deluxe	$67,000	$1145	$1355

Prices Subject to Change Without Notice.

St. Mark Village

2655 Nebraska Ave. (S.R. 584-A), just east of U.S. 19
Palm Harbor, Florida 34684, Ph. 813/785-2576



Bright, de

Gardens t



Friends,



Sport Fishing Institute

Chris - caring about fish issues does play well. DH

1010 Massachusetts Ave., N.W., Suite 100, Washington, D.C. 20001 (202) 898-0770

January 13, 1989

cc: David Dennard
Curt Smith
FYI / BdG.

Mr. James D. Range
Government Affairs
Waste Management, Inc.
1155 Connecticut Avenue, N.W.
Suite 800
Washington, D.C. 20036

[redacted]

Dear Jim:

President-Elect Bush has publicly demonstrated his interest in the environment and fisheries by word and deed. Clearly, he believes that fishing is an important part of the quality of his life. One quarter of the people of this nation, 60 million Americans, join him in supporting this belief -- they too are fishermen. In addition, the fisheries resource base supports more than a million jobs and $60 million in economic activity per year. Immeasurable social benefits in recreation and nutrition are dependent on our nation's fisheries resource.

The quality of fishing reflects the quality of living. Fish are indicator organisms reflecting the condition of the environment. The President-Elect linked the quality of the environment to funds made available through the Wallop-Breaux amendments to the Federal Aid in Sport Fish Restoration Act, the passage of which he supported. We too feel fish are "the canary in the mine" as far as the health of aquatic systems are concerned. Ocean dumping has resulted in fish unfit for human consumption. Acid rain has eliminated fish populations from lightly buffered aquatic systems in the northeast. Point and non-point pollution of our nation's streams, lakes and estuaries have degraded fish habitats and reduced the productivity of these systems. Finally, the continuing loss of wetlands is destroying critical fish nursery habitat for more than 70 percent of our nation's economically important species.

We call on the President to prominently and publicly state his intention to lead the nation in cooperative action agenda to restore the health of our nation's fisheries.

Jim, is there any way we can get this information to Mr. Bush's speech writers? We sure would like him to make reference to angling in his upcoming speeches. The pictures of Mr. Bush in Newsweek and Time were great? It makes him more "folksy" and the common man can relate to a fellow angler.

Sincerely yours,

Gil

Gilbert C. Radonski
President

GCR/nah

The National Non-Profit Fish Conservation Organization

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Chicago, IL

DANA PICKUP
Cuba Speciality Mfrg. Co.
Fillmore, NY

DAVID PORTHOUSE
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Chesterfield, MO

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Silstar Corp. of America
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HELEN SEVIER
B.A.S.S.
Montgomery, AL

ARTHUR SHAPIRO
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TASK FORCE ON CRIME

Congress of the United States
House of Representatives
Washington, DC 20515-0909

PLEASE RESPOND TO:

WASHINGTON OFFICE:
☐ 1530 LONGWORTH HOUSE OFFICE BUILDING
WASHINGTON, DC 20515-0908
(202) 225-5755

DISTRICT OFFICES:
☐ 1100 CLEVELAND STREET, SUITE 1500
CLEARWATER, FL 34615
(813) 441-3721

☐ 2739 U.S. HWY. 19, SUITE 110
HOLIDAY, FL 34691
(813) 947-1022

☐ 408 WEST RENFRO STREET
SUITE 107F
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(813) 752-9260

DATE 4/24/89 TIME _____

Total number of pages including the cover page: 10 pages

Please deliver to

Name: Rhett (Speedwriting)

Telephone/Telecopier number: _____

From

Name: Bob Meyers (Cong. Bilirakis)

Telephone/Telecopier number: 225-5755

Comments

ATTACHED IS ① original memo to ADVANCE ② info on Cong. Bilirakis + Alzheimer's Disease

1 of 9

4/24 Rhett - This has changed as to format - primarily due to time limits - now - it looks like only 20 minutes or so @ the facility

Bob Meyers

MEMORANDUM

TO: White House Advance

FROM: Bob Meyers (Rep. Bilirakis)
225-5755 (w) 703-549-0132 (h)

RE: President's visit to St. Mark Village, Palm Harbor, Florida

DATE: 4/21/89

Purpose of Visit:

The President will be visiting Palm Harbor to participate in a ceremony to dedicate the "Michael Bilirakis Alzheimer's Center". The center contains nursing and "assisted living" quarters specifically designed for the care of Alzheimer's Disease patients.

The center was named after Congressman Bilirakis to recognize his long interest and legislative activity with regard to Alzheimer's Disease. The Congressman introduced successful legislation to provide for Medicare demonstration projects for Alzheimer's Disease as well as family support groups.

The Michael Bilirakis Alzheimer's Center is located at St. Mark Village, a congregate living facility. At present, the center contains 20 nursing beds and 31 assisted living apartments for those afflicted with Alzheimers. Altogether, St. Mark Village contains 324 living units and approximately 500 residents. St. Mark Village is a not-for-profit independent corporation founded by the St. Mark Lutheran Church of Dunedin, Florida.

Outline of the Event:

A proposed timeline for the President's visit is attached. In general, it is contemplated that there will be a ceremony on stage at which the President will make some brief remarks commenting on: (a) Congressman Bilirakis and his work in the area of Alzheimer's Disease and (b) the President's concern for adequate health care for the elderly -- especially with regard to debilitating diseases like Alzheimers.

2 of 9

I have attached separate talking points on both (a) and (b). More broadly on these points -- we feel the dedication presents a good opportunity for the President to draw national attention to Alzheimer's Disease and health care for the elderly. Nearly 500 elderly people live at St. Mark Village -- and the new center is one of the few in the country specifically designed for A.D. Therefore, the "backdrop" is excellent for any remarks or message of this kind.

Participants on Stage:

At present, only the following people are contemplated to be on stage with the President:

(1) Congressman Bilirakis, his wife, Evelyn and their son, Gus.

(2) Ed Hutfliz, Executive Director of St. Mark and his wife.

(3) Pastor Fresh, President of the Board, St. Mark Village and his wife.

(4) Governor Martinez (possible)

(5) Representative Bill Young (possible)

(6) Senator Connie Mack and Senator Bob Graham (invited)

Audience:

The size of the audience will depend on the determination of the White House advance team as to whether the St. Mark courtyard is a suitable location -- or whether the event must be held in the auditorium. The auditorium seats approximately 300 people. The courtyard will accomondate several hundred to over 1,000 people.

In any event -- the composition of the audience will be: (a) residents of St. Mark Village who are physically able to attend (the event will be transmitted through television to those who are "room bound." (b) local Republican officials, committemen, supporters of President Bush and Congressman Bilirakis, (c) local senior group members and officials included NARFE and AARP.

As a gauge to crowd size -- town meetings which Congressman Bilirakis has held in this area have exceeded 800 people. The surrounding area is filled with large retirement communities and apartment complexes. Given the publicity the event will receive, the natural expectation would be for a large turnout.

3 of 9

Reception:

A reception for approximately 100 people is also planned for the event. Participants at this event would primarily be: St. Mark Board of Directors, local officials and close supporters of Congressman Bilirakis. Planning would include opportunity for photographs.

Media:

In addition to media traveling with the President, the expressed interest of the local television, radio and newspapers is exceedingly high. President Bush is very popular in Pinellas County (which maintains the highest number of Republican registrants in the state). To the extent possible, we would want to provide access for our local press.

Plauqes -- President:

As part of the dedication ceremony, we would like to request that the President present a plaque to Congressman Bilirakis and Pastor Fresh, Chairman of the Board, St. Mark Village. Under the proposed schedule, the plaques would be presented following the President's remarks.

President's Remarks:

Two memos have been attached which outline (a) Congressman Bilirakis' work on Alzheimer's Disease and (b) the disease generally.

As you may know, Alzheimer's Disease extracts a heavy toll from both the patient -- who gradually becomes disoriented and incapable of caring for him or herself -- and the family which seeks to care for the patient and has the exceedingly stressful experience of watching a loved one undergo this transformation.

Therefore, if there is any one overriding theme to this event, it is one of compassion and caring. Right now, there is no cure for Alzheimer's Disease although research is ongoing. Therefore, the primary challenge is one of care for the patient and support for the family.

Alzheimer's is a terrifying disease which extracts a heavy toll from society. The President's remarks should reflect this somber fact.

4/89

CONGRESSMAN BILIRAKIS' WORK ON ALZHEIMERS DISEASE

*

Florida's Ninth District has one of the highest concentrations of elderly citizens in the country, thus the prevalence of Alzheimer's Disease is very high there as it is a disease which afflicts individuals in the mid to late-life years.

* Congressman Bilirakis always has been active legislatively regarding Alzheimer's Disease.

98th Congress:

* Introduced a bill directing HHS to set up a network of family support groups in universities and other facilities that were receiving federal funds for Alzheimer's research. These support groups would help victims in the early stages of Alzheimer's Disease. They would also help the family members to cope with the ravages of Alzheimer's Disease on their loved one.

* Introduced a bill calling for the establishment of 10 one-year demonstration projects to determine the feasibility of providing Medicare assistance for Alzheimer's Disease. Alzheimer's Disease often can take as long as 20 years to run its course, thus the financial implications for a family with an Alzheimer's patient can be devastating.

99th Congress:

* As Florida's only member on the Energy and Commerce Committee's Health and Environment Subcommittee, he steered both bills through the Congress to passage into law. The first bill was passed as an amendment to the Protection and Advocacy Services for the Mentally Ill Persons Act of 1986. The demonstration projects also were passed and became Public Law 99-509.

While Congressman Bilirakis proposed 10 one-year projects, the law calls for the establishment of five three-year demonstration projects. HHS is in the process of beginning these projects.

Current:

* Congressman Bilirakis annually cosponsors legislation designating November of each year as "Alzheimer's Disease Awareness Month."

* Congressman Bilirakis always lends his assistance to local Alzheimer's Disease projects. He has assisted the Alzheimer's Disease Support Groups and aided the Pasco County Sheriff's Department in its goal of providing identification bracelets for Alzheimer's Disease patients. He has visited institutionalized patients who are stricken with Alzheimer's Disease.

* In recognition of his efforts for Alzheimer's Disease patients and their families, St. Mark's Village has chosen to honor him by naming its new facility the Mike Bilirakis Alzheimer's Wing.

# # # # #

599

TALKING POINTS ON ALZHEIMERS DISEASE

Background:

* Alzheimer's Disease was discovered in 1906 by Alois Alzheimer, a German neurologist. It is a progressive disease of the brain affecting memory, thought processing and language. **It is the fourth leading cause of death in the elderly. There is no cure.**

More than four million persons are now affected by Alzheimers Disease. By the year 2000, it is projected that 7.4 million people will be affected by the disease. At that time, as much as a quarter of the U.S. population will be over 50 and will be at some risk of being stricken by the disease. About one of eight will be 65 or older and at heightened risk.

With the increase in the elderly population, we will get a corresponding increase in the number of people who will be afflicted by the disease unless a cure is found.

* Victims of the disease are individuals of either sex who are usually beyond their mid-life years. Alzheimers may often take as long as 20 years to run its course.

Changes occur gradually in the brain cells and at first symptoms are barely noticeable. As the disease progresses, memory loss progresses to a significant degree and there are other changes in behavior that can result in lead an individual degenerating into a vegetative state.

* When an Alzheimer's victim dies, the disease isn't normally listed on the death certificate as a cause of death because persons don't die from brain cells not functioning. However, persons in vegetative states (as a result of Alzheimer's Disease) can develop serious infection resulting in death.

Possible Causes Of Alzheimer's:

1.) Genetic Factors -- includes familial (a pattern in a family suggesting the disease is inherited) aggregation, association with Down's syndrome, and altered DNA-binding proteins.

2.) Exaggerated Aging -- symptoms of the disease such as senility and dementia, are not part of the normal aging process.

3.) Environmental Factors -- includes metal exposures, head trauma, viruses and other infectious agents.

4.) Immunologic Factors -- includes special susceptibility to infectious agents reacting with one's own brain cells.

5.) Disrupted nerve cell circuits -- includes loss of specific populations of nerve cells and disruption of communication between certain groups of brain cells.

6.) Intrinsic Metabolic Factors -- includes disruption of biochemical pathways in brain cells.

6 of 9

Financial Impact On Families:

Devastating, primarly because Alzheimers patients aren't covered under the Medicare program. Approximately $80 million is spent annually on the cost of care for Alzheimers Disease.

Treatment:

Virtually non-existent. FDA is conducting clinical trials across the nation on THA, a drug that allegedly depresses enzymes that destroy the brain transmitter, which has deteriorated as a result of the disease. The brain transmitter allows cells to communicate with each other. While preliminary studies have conflicting results about the effects of THA, FDA is still funding clinical trials on THA. Currently, 300-400 people are participating in these trials.

Government Funding:

Research only. Congress approved an increase in federal funds being spent on Alzheimer's Disease research to $120 million in FY89. This is a 32% increase over FY88, but amounts to just $30 per patient.

# # # # #

7 of 9

Mike Bilirakis was first elected to Congress on November 2, 1982, defeating Democrat George Sheldon in a closely contested race.

In 1984 and 1986, however, Mike Bilirakis soundly defeated his Democratic challengers, drawing broad support from all areas of the Ninth Congressional District -- a district that spans northern Pinellas, Pasco and parts of Hillsborough Counties.

Mike was born in the Ninth District, in Tarpon Springs, on July 16, 1930. Shortly after his birth, however, Mike's Greek immigrant parents, Emmanuael and Irene, left the area for Pennsylvania.

Early in life, Mike developed a "work hard and work your way up philosophy". He experienced poverty as a young man, but he always had a clear vision of a better future. He knew that to "play with the cards he had been dealt" he would not be able to provide for his family in the manner he desired. The only course available was to work his way up the ladder.

899

Growing up in Pittsburgh, then, Mike worked hard in the steel mills, saving money he would later need for college. He worked the night shift to pay his way to an engineering degree at the University of Pittsburgh and later, he also graduated from law school at the University of Florida.

After several varied jobs, including work on an oil rig in the Gulf of Mexico and with a local aerospace firm, Mike opened his own law practice in Holiday in 1969. He later invested in land and small businesses and taught several courses at local community colleges. In addition, Mike accepted appointments as county and municipal judge, traveling often to Dade City to preside over cases.

Today, Mike's diverse background and experience are paying off for residents of the Ninth Congressional District as he continues his work habits as a three-term incumbent. Mike is perhaps the only petroleum engineer in the U.S. Congress -- important to his work on the Energy and Commerce Committee.

9/9

As a veteran and member of the House Veterans Affairs Committee, Mike also has taken an active role in veterans legislation. His work helped to bring a new V.A. outpatient clinic to Pasco County, and and he has hosted several veteran committee meetings and workshops in the district. Mike has also taken a keen interest in the matter of American POWs and MIAs in Southeast Asia, having traveled to Vietnam and Laos in pursuit of new information on our missing veterans.

Mike's tough-minded philosophy is also paying off for his family as his two sons pursue advanced degrees. Currently, his son Manuel is studying medicine at the University of Miami while Gus is a law student at Stetson University in DeLand.

Along with his wife, Evelyn, Mike travels throughout the Ninth District at every opportunity. Fulfilling a campaign promise made long ago, Mike continuously visits local groups and listens to citizens, seeking always to be a "true representative of the people."

Dedication of Wing (1 – 3Pm.)

1Pm Program start

130 Pres. arrives

140 Pres. announced onto to stage.

1.45 Cong. Bilirakis ~~on~~ introduces the Pre

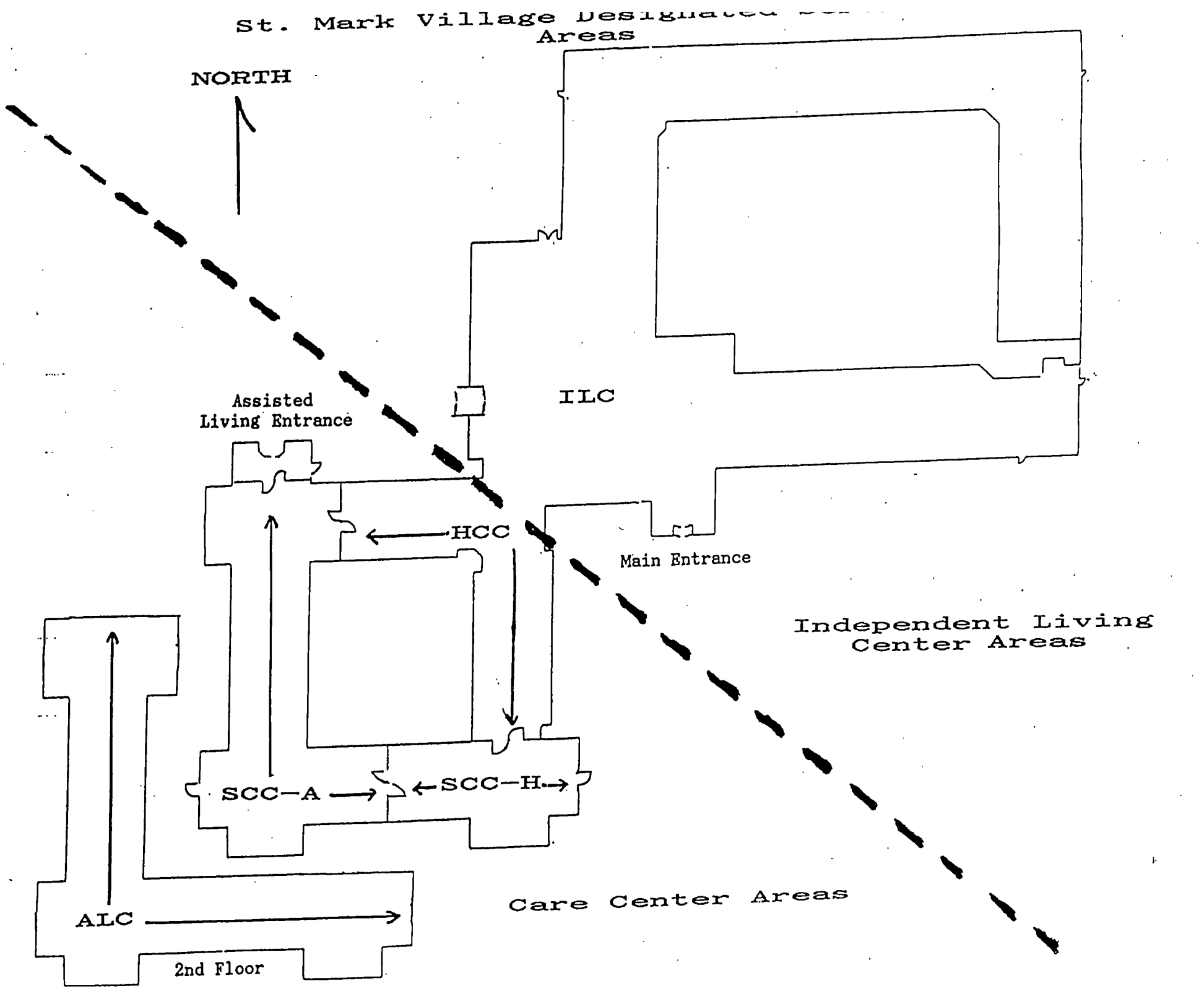
1.50 The Pres. makes remarks

155 The Pres. proceeds to VIP reception – 100pp – (20 minutes)

215 Tour of the facility (20 minutes)

235 The Pres. depart facility to airport

Jim Loy.
267-2380
323-7310


St. Mark Village Designated
Areas
NORTH
ILC
Assisted
Living Entrance
HCC
Main Entrance
Independent Living
Center Areas
SCC—A
SCC—H
ALC
2nd Floor
Care Center Areas

aer/10-88

TALKING POINTS -- ALZHEIMER'S DISEASE

Mike has been a leading advocate of assistance for Alzheimer's disease patients and their families.

100th Congress

August 1988: St. Mark Village opened an Alzheimer's center named for Mike Bilirakis in recognition of the work he has done and will do in the future for individuals suffering from Alzheimer's Disease.

August 1988: MB provided support for "ID Bracelets for Alzheimer's Disease Patients", a project of the Alzheimer's Disease Support Group and the Pasco County Sheriff Department.

June 1988: Mike cosponsored H.J.Res. 449, a joint resolution designating the month of November 1988 as "National Alzheimer's Disease Month", which is currently pending in the Post Office and Civil Service Subcommittee on Census and Population.

November 1987: Mike cosponsored H.R. 1451, The Older American Amendments of 1987, which was signed into law (P.L. 100-175) on November 27, 1987.

Authorizes the Director of the National Institute on Aging to conduct clinical trials on the use of drugs in the treatment of Alzheimer's Disease. Authorizes appropriations for such trials for FY 1988.

Requires the secretary to make from 3 to 5 three year grants to states for demonstration projects providing a broad range of services to individuals suffering from Alzheimer's Disease or other related disorders and to their families and care givers.

99th Congress

MB introduced H.R. 66 and H.R. 67, The Alzheimer's Relief Package

These bills would establish family support groups and Alzheimers Disease demonstration projects respectively.

Substance of H.R. 66 (family support groups bill) was accepted as an amendment in Committee to H.R. 4055, The Protection and Advocacy Services for Mentally Ill Persons Act of 1986.

H.R. 4055, MB sponsored with Waxman, passed the House on January 30, 1986 (290-84). The Conference Report passed on May 13, by a vote of 383-21. The Conference Report, also was on S.974, Senator Weicker's P&A bill (companion to H.R. 4055). The Conference Report was signed into law (P.L. 99-319) on May 23, 1986.

The family support groups would be established in health care facilities receiving federal funds for Alzheimer's research.

H.R. 5300, now (P.L. 99-509) incorporated H.R. 67 which provided authority for five 3 year demonstration projects to be established in order to determine the feasibility of extending Medicaid assistance for Alzheimer's Disease victims.

AUG 12 1988

DATE: August 10, 1988

FOR IMMEDIATE RELEASE:

St. Mark Village opens the Michael Bilirakis Alzheimers Care Center.

CONTACT:

Al Simpson
Director of Public Relations
St. Mark Village
2655 Nebraska Avenue
Palm Harbor, FL 34663
(813) 785-2576

St. Mark Village of Palm Harbor is pleased to announce the pending opening of the Michael Bilirakis Alzheimers Center and a special division of "assisted living" apartments.

The Alzheimers Care Center is named for Congressman Michael Bilirakis, U.S. House of Representatives, Ninth District of Florida, in recognition of his continuous effort to address the needs and problems of the aging population, particularly those suffering from Alzheimers and related dementia disorders.

The first floor of the new, two story addition is dedicated to the care of Alzheimers sufferers. It will consist of 20 nursing beds and 31 special assisted living apartments. "We believe it to be the first such facility in the nation designed to provide care for patients with Alzheimers Disease and other types of dementia, from the beginning diagnosis through terminal stages of the illness," said Allan Simpson, Director of Public Relations for St. Mark Village. Statistics indicate approximately 20 percent of the population over age 80 suffer from some type of dementia disorder, and 60 percent of these are in some stage of Alzheimers." Simpson continued, noting that "more than 100,000 die of Alzheimers Disease annually which makes it the fourth leading cause of death in adults, after heart disease, cancer, and stroke."

Also opening is a new health care division of the Village. This 34 apartment assisted living unit is designed for those physically impaired who need extra assistance with medicines and personal care. The aim is to provide the greatest degree of personal freedom possible in beautiful homelike surroundings.

While all facilities are primarily for the continuing care of St. Mark Village residents, the added capacity will be available to people in the Tampa Bay Area as well. It is also expected that short term respite care will be made available in the Bilirakis Alzheimer's Center.

St. Mark Village is a not-for-profit independent corporation founded by the St. Mark Lutheran Church of Dunedin. It receives no tax based support or assistance. Regulated by Florida H.R.S. and other regulating authorities, it maintains a superior rating.

The entire complex, including the eight year old apartment building and regular nursing center have been completely renovated and redocorated as part of the expansion program.

Its 11.5 acre campus offers residents deluxe studio, one and two bedroom apartments, each with complete kitchen and screened patio. Residents pay an admission fee based on the size of an apartment plus monthly maintenance fees ranging from $580 up depending on apartment size and occupancy (singles or double). The monthly fee provides one full meal daily (three are available), weekly maid service, 24 hour security and emergency nursing call, all utilities, pool, transportation and many other amenities. A skilled and caring staff free the resident from the daily routines of caring for the home to allow full and free enjoyment of the aging years.

November 4, 1988
To: Mike
From: Anne

TALKING POINTS -- ALZHEIMER'S DISEASE

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June 1988: Mike supported the rule Governing debate on H.R. 3436, the Pepper/Roybal Home Care Bill. By a vote of 169 to 243, the U.S. House of Representatives voted down H.R. 3436, a measure that would have extended Medicare home health coverage to millions of Americans, young and old, who suffer from AD and other chronic illnesses or disabilities. Had H.R. 3436 become law, it would have gone a long way towards helping AD families with the provision of home care.

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H.R. 4055, MB sponsored with Waxman, passed the House on January 30, 1986 (290-84) and subsequently laid upon the table. The House on (1/30/86) attached H.R. 4055 as an amendment to S. 974, Senator Weicker's Protection and Advocacy bill. The Conference Report passed on May 13, by a vote of 383-21. The Conference Report was signed into law (P.L. 99-319) on May 23, 1986.

Title IV of P.L. 99-319 amends title III of the Public Service Act to direct the Secretary to promote family support groups for Alzheimer's disease patients and their families, and establish a nationwide network to coordinate such groups.

NOVEMBER 4, 1988 UPDATE ON FAMILY SUPPORT GROUPS:

This family support group program was never implemented by NIMH because NIA already has funding for a very similar program. P.L. 99-660 directed NIA to establish a clearinghouse for services for victims of Alzheimer's Disease and their families. NIA is currently contracting with outside agencies for such services.

H.R. 5300, now (P.L. 99-509) incorporated H.R. 67 which provided authority for five 3 year demonstration projects to be established in order to determine the feasibility of extending Medicaid assistance for Alzheimer's Disease victims.

NOVEMBER 4, 1988 UPDATE ON DEMONSTRATION PROJECTS:

The bureau of Program Operations has conducted site visits and narrowed the number of possible sites to nineteen. Recommendations were made to Dr. William L. Roper, Administrator, Health Care Financing Administration (HCFA) in October. Within the next two weeks, Dr. Roper will select at least five demonstration sites and no more than ten.

Pg 1

President may visit Pinellas

Bilirakis wants Bush for center dedication

By TERESA BURNEY
Times Staff Writer

PALM HARBOR — President George Bush may visit Palm Harbor next week, an official said as he held his breath, crossed his fingers and knocked on wood.

U.S. Rep. Michael Bilirakis, R-Fla., has been trying to get a president to Palm Harbor to dedicate the wing for Alzheimer's disease patients at the St. Mark Village retirement center since Ronald Reagan was in office, said David White, the congressman's press secretary.

White confirmed Wednesday that Bush might be able to make it to Palm Harbor next week to dedicate the wing during a visit to Florida.

The wing is open and is named after Bilirakis.

"We are not really supposed to say anything because nothing has been firmed up," White said. "It could fall through."

Other plans to bring presidents to Palm Harbor have.

Bilirakis tried to get Reagan there for the retirement center dedication when he was president and that failed, White said.



GEORGE BUSH

"Several times we went down that primrose path and got caught by a thorn," White said.

But this time the plans have gone further than before, White said.

However, the president's advance team, which travels ahead of the president to make sure that he can safely visit places, has not visited Pinellas County and it could nix the plans.

Sean Walsh of the White House Press Office said that the president's schedule for his visit to Florida had

Please see BUSH Page 8

Bush from Page 1

not been completed Wednesday.

"We haven't announced any such plans" to visit the Palm Harbor retirement center, Walsh said.

Walsh said the president is planning a trip to California and Texas that will end in Florida next Wednesday and Thursday.

St. Mark retirement center has not been given a final answer yet, either, said Michael Spong, the center's marketing and public relations director.

"We are not ruling out the possibility of President Bush coming here but I haven't gotten anything final yet," Spong said.

Bush visit is in the works

Clwt Sun Pg 1A

BY ANN BAKKALAPULO
Staff writer

President Bush may be making a special visit to Palm Harbor next Thursday for the dedication of the Alzheimer's Center at St. Mark Village.

Bush has been asked to dedicate the Alzheimer's Center in honor of U.S. Rep. Mike Bilirakis of Tarpon Springs. Chances are good the president will be there for the ceremony, officials said.

PRESIDENT BUSH

MIKE BILIRAKIS

"Nothing is written in stone, but I think the chances are pretty good," said Dave White, a spokesman for Bilirakis. "It looks like President Bush will make it down."

The White House "advance team" must first determine if the area is secure enough for a visit from Bush, White said. That determination may come as early as today.

"Bilirakis invited the president because Alzheimer's disease has been an emerging subject for the past five or six

Please see • BUSH, page 4A

*

BUSH

CONTINUED FROM PAGE 1A

was opened in December. The center is designed for the care and treatment of people with Alzheimer's disease and other related disorders, said Edgar Hutfilz, executive director of St. Mark Village.

Alzheimer's disease is a degenerative mental disorder common among elderly people. It is gradual and results in many different types of symptoms, including incognizance and memory loss.

"The disease affects a lot of people and needs a lot of attention," said White. "The president's visit is one way of trying to rectify this problem and end the suffering. It's important to keep the issue publicized and keep the president aware of it."

Hutfilz said he would be "very excited to have the president dedicate the center because it would show the public the seriousness of the disease."

"It will be dedicated to Bilirakis because he has shown a lot of concern for this disease and wants to do anything for a cure," Hutfilz said.

years, and it is a very important issue for a large segment of the population," White said.

St. Mark Village, 2655 Nebraska Ave., is a non-profit, full-service retirement center. The Alzheimer's Center, a separate wing in St. Mark Village,

OBITUARIES

Bush coming to Palm Harbor to open Alzheimer's center

Section B - pg - 1

By RAY LOCKER and BRUCE DUDLEY
Tribune Staff Writers

WASHINGTON — President Bush will dedicate an Alzheimer's disease care center in Palm Harbor on next Thursday, the final stop in a four-day trip in which he will promote his legislative proposals, congressional and White House sources said Wednesday.

Details for the Palm Harbor stop have not been completed, said U.S. Rep. Mike Bilirakis, but Bush is expected to arrive in the afternoon after an appearance in Miami.


Bush

"It looks like it's definitely on his schedule," Bilirakis said.

Bilirakis said Bush will appear at the St. Mark's Village retirement center in Palm Harbor to open the Mike Bilirakis Alzheimer's Wing, the first treatment center of its kind in the nation.

Ed Hutfilz, St. Mark's executive director, said the wing was named for Bilirakis because of his extensive work on issues concerning Alzheimer's and the elderly.

"We felt it was an appropriate tribute for the work he has done," Hutfilz said.

Members of a White House advance team are expected to arrive in Palm Harbor today to examine St. Mark's Village for security and to determine the best place for Bush to speak, Bilirakis aides said.

Bilirakis, a Palm Harbor Republican, is a member of the House Energy and Commerce Committee's Health and the Environment Subcommittee, which handles elderly health care issues.

Bush's Florida stops next week will touch on two key issues to the state — drugs and the elderly. In Miami, Bush will participate in a drug forum with officials from the United States Coast Guard, Customs Service and the Drug Enforcement Administration.

The Bush tour begins Monday in Chicago, where he will address the American Newspaper Publishers Association. Then he will fly to Palo Alto, Calif., where he will speak Tuesday morning.

Bush will stop Tuesday night in Los Angeles to meet with former President Ronald Reagan. Bush will speak to the Texas Legislature in Austin on Wednesday and then fly to Miami for his two Florida appearances the next day.

Gov. Bob Martinez is heading a group of Republican officials who are expected to be traveling with Bush when he visits Florida.

"We're making preparations for the governor to be with him for most of the day," said Brian Ballard, the governor's operations director.

Rep. C.W. Bill Young of Seminole said he is planning to be with the president but it will depend on what legislation is being considered by the House on Thursday.

"Our ties with him are long established," Young said, pointing out that he backed Bush when he ran against Reagan for the presidency in 1980.

Predicting that Bush will be making more visits to Florida, Young said, "He appreciates Florida because we gave him the best vote in the election."

Impact fee

as the country's most urgent risk
health problem. Only 14 percent don

Alzheimer center set to open

BY JUDI MIDDLETON
Staff writer

PALM HARBOR — The only Pinellas County live-in center designed to care for victim's of Alzheimer's disease is set to open soon in St. Mark Village.

And the Mike Bilirakis Alzheimer's Center also is only the second facility in Florida specifically designed to treat Alzheimer's patients, according to St. Mark Village officials.



MIKE BILIRAKIS

The two-story addition to the village's 324-unit congregate living facility on Nebraska Avenue consists of 20 nursing beds and 31 assisted-living beds on the first floor Alzheimer's section.

The second level holds 34 apartments for people without Alzheimer's disease who nonetheless need assisted-living quarters.

"We named the center to honor Mr. Bilirakis (Republican congressman from Palm Harbor) because of all the work he has done to get the center off the ground," said Yeurith Way, resident liason at St. Mark Village.

"He has been very interested in the center from the beginning, and served as guest speaker at several of the functions we held during the planning of the center."

Mrs. Way said the Alzheimer center features hospital-type rooms for Alzheimer patients who need advanced care. It also has apartment-style living arrangements for those who have not reached that stage, but need assistance.

It will afford its residents constant medical attention, if necessary, with nurses and nursing aides on duty 24 hours a day.

"And doctors will be on the premises three days per week, and on call all the time," Mrs. Way said.

An Alzheimer patient needing advanced care will pay $75 per day for a semi-private room or $90 per day for a private room. For assisted-living in the Alzheimer's section, a resident will pay $1,600 per month for semi-private accomodations, and $1,950 for a private room. The prices include all meals and maid service.

Those wishing information about the Mike Bilirakis Alzheimer's Center may call 785-2576.

CLEARWATER SUN
AUGUST 6 1988

Dedication of Wing (1 – 3pm.)

1pm Program start
1:30 Pres. arrives
1:40 Pres. announced onto to stage
1:45 Cong. Bilbray ~~on~~ introduces the Pres

1:50 The Pres. makes remarks
1:55 The Pres. proceeds to VIP reception – 100pp –
(20 minutes)

2:15 Tour of the facility
(20 minutes)

2:35 The Pres. depart facility to airport

Jim Loy.
267-2380
323-7310

Alzheimer's

Thursday?

Sugar Ray Robinson died of Alzheimer's

ADVANCE
27565

call Advance re: Clearwater
Kelly Walker ♂ arrive Sat or Sun.
(813) 942-2000*
Centrex 5548

* BUSH HQ "Peter Hamilton"
x 3340

— dedication of a wing of a nursing home?

St. Marks
Palm Harbor