

# Alzheimer's Disease

## I INTRODUCTION

Alzheimer's Disease, progressive brain disorder that causes a gradual and irreversible decline in memory, language skills, perception of time and space, and, eventually, the ability to care for oneself. First described by German psychiatrist Alois Alzheimer in 1906, Alzheimer's disease was initially thought to be a rare condition affecting only young people, and was referred to as presenile dementia. Today late-onset Alzheimer's disease is recognized as the most common cause of the loss of mental function in those aged 65 and over. Alzheimer's in people in their 30s, 40s, and 50s, called early-onset Alzheimer's disease, occurs much less frequently, accounting for less than 10 percent of the estimated 4 million Alzheimer's cases in the United States.

Although Alzheimer's disease is not a normal part of the aging process, the risk of developing the disease increases as people grow older. About 10 percent of the United States population over the age of 65 is affected by Alzheimer's disease, and nearly 50 percent of those over age 85 may have the disease.

Alzheimer's disease takes a devastating toll, not only on the patients, but also on those who love and care for them. Some patients experience immense fear and frustration as they struggle with once commonplace tasks and slowly lose their independence. Family, friends, and especially those who provide daily care suffer immeasurable pain and stress as they witness Alzheimer's disease slowly take their loved one from them.

## II SYMPTOMS

The onset of Alzheimer's disease is usually very gradual. In the early stages, Alzheimer's patients have relatively mild problems learning new information and remembering where they have left common objects, such as keys or a wallet. In time, they begin to have trouble recollecting recent events and finding the right words to express themselves. As the disease progresses, patients may have difficulty remembering what day or month it is, or finding their way around familiar surroundings. They may develop a tendency to wander off and then be unable to find their way back. Patients often become irritable or withdrawn as they struggle with fear and frustration when once commonplace tasks become unfamiliar and intimidating. Behavioral changes may become more pronounced as patients become paranoid or delusional and unable to engage in normal conversation.

Eventually Alzheimer's patients become completely incapacitated and unable to take care of their most basic life functions, such as eating and using the bathroom. Alzheimer's patients may live many years with the disease, usually dying from other disorders that may develop, such as pneumonia. Typically the time from initial diagnosis until death is seven to ten years,

but this is quite variable and can range from three to twenty years, depending on the age of onset, other medical conditions present, and the care patients receive.

### III BRAIN ABNORMALITIES

The brains of patients with Alzheimer's have distinctive formations—abnormally shaped proteins called tangles and plaques—that are recognized as the hallmark of the disease. Not all brain regions show these characteristic formations. The areas most prominently affected are those related to memory.

Tangles are long, slender tendrils found inside nerve cells, or neurons. Scientists have learned that when a protein called tau becomes altered, it may cause the characteristic tangles in the brain of an Alzheimer's patient. In healthy brains, tau provides structural support for neurons, but in Alzheimer's patients this structural support collapses.

Plaques, or clumps of fibers, form outside the neurons in the adjacent brain tissue. Scientists found that a type of protein, called amyloid precursor protein, forms toxic plaques when it is cut in two places. Researchers have isolated the enzyme beta-secretase, which is believed to make one of the cuts in the amyloid precursor protein. Researchers also identified another enzyme, called gamma secretase, that makes the second cut in the amyloid precursor protein. These two enzymes snip the amyloid precursor protein into fragments that then accumulate to form plaques that are toxic to neurons.

Scientists have found that tangles and plaques cause neurons in the brains of Alzheimer's patients to shrink and eventually die, first in the memory and language centers and finally throughout the brain. This widespread neuron degeneration leaves gaps in the brain's messaging network that may interfere with communication between cells, causing some of the symptoms of Alzheimer's disease.

Alzheimer's patients have lower levels of neurotransmitters, chemicals that carry complex messages back and forth between the nerve cells. For instance, Alzheimer's disease seems to decrease the level of the neurotransmitter acetylcholine, which is known to influence memory. A deficiency in other neurotransmitters, including somatostatin and corticotropin-releasing factor, and, particularly in younger patients, serotonin and norepinephrine, also interferes with normal communication between brain cells.

### IV CAUSES

The causes of Alzheimer's disease remain a mystery, but researchers have found that particular groups of people have risk factors that make them more likely to develop the

disease than the general population. For example, people with a family history of Alzheimer's are more likely to develop Alzheimer's disease.

Some of the most promising Alzheimer's research is being conducted in the field of genetics to learn the role a family history of the disease has in its development. Scientists have learned that people who are carriers of a specific version of the apolipoprotein E gene (apoE gene), found on chromosome 19, are several times more likely to develop Alzheimer's than carriers of other versions of the apoE gene. The most common version of this gene in the general population is apoE3. Nearly half of all late-onset Alzheimer's patients have the less common apoE4 version, however, and research has shown that this gene plays a role in Alzheimer's disease. Scientists have also found evidence that variations in one or more genes located on chromosomes 1, 10, and 14 may increase a person's risk for Alzheimer's disease. Scientists have identified the gene variations on chromosomes 1 and 14 and learned that these genes produce mutations in proteins called presenilins. These mutated proteins apparently trigger the activity of the enzyme gamma secretase, which splices the amyloid precursor protein.

Researchers have made similar strides in the investigation of early-onset Alzheimer's disease. A series of genetic mutations in patients with early-onset Alzheimer's has been linked to the production of amyloid precursor protein, the protein in plaques that may be implicated in the destruction of neurons. One mutation is particularly interesting to geneticists because it occurs on a gene involved in the genetic disorder Down syndrome. People with Down syndrome usually develop plaques and tangles in their brains as they get older, and researchers believe that learning more about the similarities between Down syndrome and Alzheimer's may further our understanding of the genetic elements of the disease.

Some studies suggest that one or more factors other than heredity may determine whether people develop the disease. One study published in February 2001 compared residents of Ibadan, Nigeria, who eat a mostly low-fat vegetarian diet, with African Americans living in Indianapolis, Indiana, whose diet included a variety of high-fat foods. The Nigerians were less likely to develop Alzheimer's disease compared to their U.S. counterparts. Some researchers suspect that health problems such as high blood pressure, *atherosclerosis* (arteries clogged by fatty deposits), high cholesterol levels, or other cardiovascular problems may play a role in the development of the disease.

Other studies have suggested that environmental agents may be a possible cause of Alzheimer's disease; for example, one study suggested that high levels of aluminum in the brain may be a risk factor. Several scientists initiated research projects to further investigate this connection, but no conclusive evidence has been found linking aluminum with Alzheimer's disease. Similarly, investigations into other potential environmental causes, such as zinc exposure, viral agents, and food-borne poisons, while initially promising, have generally turned up inconclusive results.

Some studies indicate that brain trauma can trigger a degenerative process that results in Alzheimer's disease. In one study, an analysis of the medical records of veterans of World War II (1939-1945) linked serious head injury in early adulthood with Alzheimer's disease in later life. The study also looked at other factors that could possibly influence the development of the disease among the veterans, such as the presence of the apoE gene, but no other factors were identified.

## V DIAGNOSIS

Alzheimer's disease is only positively diagnosed by examining brain tissue under a microscope to see the hallmark plaques and tangles, and this is only possible after a patient dies. As a result, physicians rely on a series of other techniques to diagnose probable Alzheimer's disease in living patients. Diagnosis begins by ruling out other problems that cause memory loss, such as stroke, depression, alcoholism, and the use of certain prescription drugs. The patient undergoes a thorough examination, including specialized brain scans, to eliminate other disorders. The patient may be given a detailed evaluation called a neuropsychological examination, which is designed to evaluate a patient's ability to perform specific mental tasks. This helps the physician determine whether the patient is showing the characteristic symptoms of Alzheimer's disease—progressively worsening memory problems, language difficulties, and trouble with spatial direction and time. The physician also asks about the patient's family medical history to learn about any past serious illnesses, which may give a hint about the patient's current symptoms.

## VI TREATMENT

There is no known cure for Alzheimer's disease, and treatment focuses on lessening symptoms and attempting to slow the course of the disease. Drugs that increase or improve the function of brain acetylcholine, the neurotransmitter that affects memory, have been approved by the United States Food and Drug Administration (FDA) for the treatment of Alzheimer's disease. Called acetylcholinesterase inhibitors, these drugs have had modest but clearly positive effects on the symptoms of the disease. These drugs can benefit patients at all stages of illness, but they are particularly effective in the middle stage. This finding corresponds with new evidence that low acetylcholine levels in patients with Alzheimer's disease may not be present in the earliest stage of the illness.

Evidence shows that there is inflammation in the brains of Alzheimer's patients, which may be associated with the production of amyloid precursor protein. Studies are underway to find drugs that prevent this inflammation, to possibly slow or even halt the progress of the disease. Other promising approaches center on mechanisms that manipulate amyloid precursor protein production or accumulation. Drugs are in development that may block the activity of the enzymes that cut the amyloid precursor protein, halting amyloid production.

Other studies in mice suggest that vaccinating animals with amyloid precursor protein can produce a reaction that clears amyloid precursor protein from the brain. Physicians have started vaccination studies in humans to determine if the same potentially beneficial effects can be obtained. There is still much to be learned, but as scientists better understand the genetic components of Alzheimer's, the roles of the amyloid precursor protein and the tau protein in the disease, and the mechanisms of nerve cell degeneration, the possibility that a treatment will be developed is more likely.

## VII CARING FOR THE ALZHEIMER'S PATIENT

The responsibility for caring for Alzheimer's patients generally falls on their spouses and children. Caregivers must constantly be on guard for the possibility of an Alzheimer's patient wandering away or becoming agitated or confused in a manner that jeopardizes the patient or others. Coping with a loved one's decline and inability to recognize familiar faces causes enormous pain.

The increased burden faced by families is intense, and the life of the Alzheimer's caregiver is often called a 36-hour day. Not surprisingly, caregivers often develop health and psychological problems of their own as a result of this stress. The Alzheimer's Association, a national organization with local chapters throughout the United States, was formed in 1980 in large measure to provide support for Alzheimer's caregivers. Today, national and local chapters are a valuable source for information, referral, and advice.