

## Understanding Alzheimer's Disease

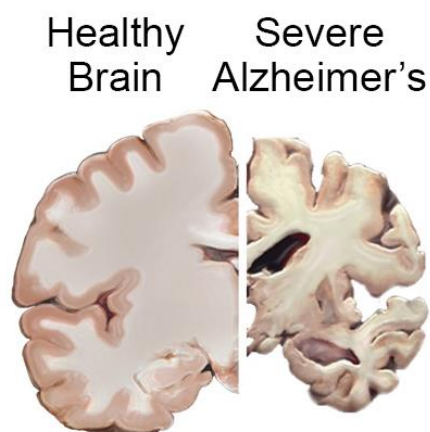
Alzheimer's disease is an irreversible, progressive brain disorder that slowly impacts memory, thinking, skills and, eventually, the ability to carry out the simplest tasks. Experts suggest that more than 5 million Americans may have Alzheimer's, nearly 65,000 of whom are living in San Diego. Alzheimer's disease is currently ranked as the sixth leading cause of death in the United States and the third leading cause of death in San Diego County.

Alzheimer's is the most common type of dementia among older adults. Dementia is the loss of cognitive functioning—thinking, remembering, and reasoning—and behavioral abilities to such an extent that it interferes with a person's daily life and activities. Other dementias include Lewy body dementia, frontotemporal disorders and vascular dementia. It is common for people to have mixed dementia—a combination of two or more disorders, Alzheimer's disease and vascular dementia is the most common.

Alzheimer's disease is named after Dr. Alois Alzheimer. In 1906, Dr. Alzheimer noticed changes in the brain tissue of a woman who had died of an unusual mental illness. Her symptoms included memory loss, language problems, and unpredictable behavior. After she died, he examined her brain and found many abnormal clumps (now called amyloid plaques) and tangled bundles of fibers (now called neurofibrillary, or tau, tangles)<sup>1</sup>.

### Changes in the Brain

Scientists continue to unravel the complex brain changes involved in the onset and progression of Alzheimer's disease. It seems likely that damage to the brain starts a decade or more before memory and other cognitive problems appear. During this preclinical stage of Alzheimer's disease, people seem to be symptom-free, but toxic changes are taking place in the brain. Abnormal deposits of proteins form amyloid plaques and tau tangles throughout the brain. The plaques and tangles prevent connections between nerve cells (neurons) in the brain. Neurons transmit messages between different parts of the brain, and from the brain to muscles and organs in the body. Once healthy neurons stop functioning and lose connections with other neurons, they die.



*Cross sections of the brain show atrophy, or shrinking, of brain tissue caused by Alzheimer's disease.*

The damage initially appears to take place in the hippocampus, the part of the brain essential in forming memories. As more neurons deteriorate, additional parts of the brain are affected, and they begin to shrink. By the late stage of Alzheimer's, damage is widespread, and brain volume has shrunk significantly.

Scientists don't yet fully understand what causes Alzheimer's disease in most people. In people with early-onset Alzheimer's, a genetic mutation is usually the cause. Late-onset Alzheimer's arises from a complex series of brain changes that occur over decades. The causes probably include a combination of genetic, environmental, and lifestyle factors. The importance of any one of these factors in increasing or decreasing the risk of developing Alzheimer's may differ from person to person.

## Stages of Alzheimer's

While the first symptoms of Alzheimer's disease vary from person to person, and the disease advances at different rates, stages provide a general guideline for understanding the progression of Alzheimer's disease. It is important to remember that each individual with Alzheimer's disease progresses differently, the time spent in each stage varies widely, and not everyone experiences all Alzheimer's disease symptoms.

### Early Stage

In the early stage, people experience changes in their short-term memory, have difficulty remembering names or words, get lost more frequently, have trouble handling money and paying bills, repeat questions, take longer to complete normal daily tasks, and exhibit personality and behavior changes. Early detection of the disease allows for individuals to be proactive and plan for their future. The average length of this stage is 2-3 years. ***\*Contact Alzheimer's San Diego about options for our Early Stage Programs.***

### Middle Stage

In the middle stage, damage occurs in areas of the brain that control language, reasoning, sensory processing, and conscious thought. People may have more difficulty communicating or following the sequence of a conversation or storyline. They may be unable to learn new things, carry out multistep tasks such as getting dressed, or cope with new situations. In addition, people at this stage may have hallucinations, delusions, and paranoia and may behave impulsively. The average length of this stage is 6-8 years.

### Late Stage

In the late stage, plaques and tangles continue to spread throughout the brain causing further atrophy (shrinkage). It becomes difficult for people to communicate and will need full assistance with activities of daily living (bathing, dressing, toileting, eating, ambulation). The body begins to prepare for end of life and separation. The average length of this stage is 2-3 years. ***\*Please note, late stage and late-onset Alzheimer's Disease are not the same thing.***

## Research Furthers Our Understanding of Alzheimer's

Scientists are conducting studies to learn more about plaques, tangles, and other biological features of Alzheimer's disease. Advances in brain imaging techniques allow researchers to see the development and spread of abnormal amyloid and tau proteins in the living brain, as well as changes in brain structure and function. Scientists are also exploring the very earliest steps in the disease process by studying changes in the brain and body fluids that can be detected years before Alzheimer's symptoms appear. Findings from these studies will help in understanding the causes of Alzheimer's and make diagnosis easier.

One of the great mysteries of Alzheimer's disease is why it largely strikes older adults. Research on normal brain aging is shedding light on this question. For example, scientists are learning how age-related changes in the brain may harm neurons and contribute to Alzheimer's damage. These age-related changes include atrophy (shrinking) of certain parts of the brain, inflammation, production of unstable molecules called free radicals, and mitochondrial dysfunction (a breakdown of energy production within a cell).

## Genetics and Genetic Testing

Most people with Alzheimer's have the late-onset form of the disease, in which symptoms become apparent in their mid-60s. The apolipoprotein E (APOE) gene is involved in late-onset Alzheimer's and has several forms. The APOE e4 form increases a person's risk of developing the disease and is also associated with an earlier age of disease onset. APOE e4 is called a risk-factor gene because it increases a person's risk of developing the disease, however inheriting an APOE e4 allele does not mean that a person will definitely develop Alzheimer's. Some people with an APOE e4 allele never get the disease, and others who develop Alzheimer's do not have any APOE e4 alleles.

Also, scientists have identified a number of regions of interest in the genome (an organism's complete set of DNA) that may increase a person's risk for late-onset Alzheimer's to varying degrees.

Early-onset Alzheimer's disease occurs in people age 30 to 60 and represents less than 5 percent of all people with Alzheimer's. Most cases are caused by an inherited change in one of three genes, resulting in a type known as early-onset familial Alzheimer's disease, or FAD. For others, the disease appears to develop without any specific, known cause. A child whose biological mother or father carries a genetic mutation for early-onset FAD has a 50/50 chance of inheriting that mutation. If the mutation is in fact inherited, the child has a very strong probability of developing early-onset FAD.

Most people with Down syndrome develop Alzheimer's. This may be because people with Down syndrome have an extra copy of chromosome 21, which contains the gene that generates harmful amyloid.

A blood test can identify which APOE alleles a person has, but results cannot predict who will or will not develop Alzheimer's disease. It is unlikely that genetic testing will ever be able to predict the disease with 100 percent accuracy, researchers believe, because too many other factors may influence its development and progression. Genetic testing is used by researchers conducting clinical trials and by physicians to help diagnose early-onset Alzheimer's disease, however, genetic testing is not otherwise recommended.

## Diagnosis of Alzheimer's

Doctors use several methods and tools to help determine whether a person who is having memory problems has "possible Alzheimer's dementia" (dementia may be due to another cause) or "probable Alzheimer's dementia" (no other cause for dementia can be found). To diagnose Alzheimer's doctors may:

- Ask the person and a family member or friend questions about overall health, past medical problems, ability to carry out daily activities, and changes in behavior and personality
- Conduct tests of memory, problem solving, attention, counting, and language
- Carry out standard medical tests, such as blood and urine tests, to identify other possible causes of the problem
- Perform brain scans, such as computed tomography (CT), magnetic resonance imaging (MRI), or positron emission tomography (PET), to rule out other possible causes for symptoms.

These tests may be repeated to give doctors information about how the person's memory and other cognitive functions are changing over time. Alzheimer's disease can be definitively diagnosed only after death, by linking clinical measures with an examination of brain tissue in an autopsy.

People with memory and thinking concerns should talk to their doctor to find out whether their symptoms are due to Alzheimer's or another cause, such as stroke, tumor, Parkinson's disease, sleep disturbances, side effects of medication, an infection, or a non-Alzheimer's dementia. Some of these conditions may be treatable and possibly reversible.

If the diagnosis is Alzheimer's, beginning treatment early in the disease process may help preserve daily functioning for some time, even though the underlying disease process cannot be stopped or reversed. An early diagnosis also helps families plan for the future. They can take care of financial and legal matters, address potential safety issues, learn about living arrangements, and develop support networks. In addition, an early diagnosis gives people greater opportunities to participate in clinical trials that are testing possible new treatments for Alzheimer's disease or other research studies.

## Treatment of Alzheimer's

Several prescription drugs are currently approved by the U.S. Food and Drug Administration (FDA) to treat people who have been diagnosed with Alzheimer's disease. Treating the symptoms of Alzheimer's can provide patients with comfort, dignity, and independence for a longer period of time and can encourage and assist their caregivers as well. It is important to understand that none of these medications stops the disease itself.

In contrast, there are some medications that can cause drowsiness, confusion, increased cognitive impairment, slowed reaction, and worsening balance leading to falls. Sleep aids usually have the same effects. Examples of sedatives to avoid include the benzodiazepines diazepam (Valium), lorazepam (Ativan), temazepam (Restoril), triazolam (Halcion), and sleep aids zolpidem (Ambien), eszopiclone (Lunesta), and zaleplon (Sonata).

Certain antidepressants, such as the older tricyclic antidepressants amitriptyline (Elavil), nortriptyline (Pamelor), and imipramine (Tofranil), can cause sedation and worsening cognition. The tricyclic antidepressants have anticholinergic effects, meaning that they can further suppress the activity of acetylcholine, one of the main brain cell messenger chemicals whose activity is reduced by Alzheimer's

disease. For low mood and irritability in patients with Alzheimer's, the SSRI (selective serotonin reuptake inhibitor) antidepressants including citalopram (Celexa), fluoxetine (Prozac), paroxetine (Paxil), sertraline (Zoloft) and the SARI (serotonin antagonist and reuptake inhibitor) such as trazodone (Desyrel) can be considered instead.

Antipsychotics are sometimes given to treat behavioral symptoms such as agitation, aggressiveness, hallucinations and delusions. However, both the older antipsychotic drugs such as haloperidol (Haldol) and the newer atypical antipsychotics such as risperidone (Risperdal), olanzapine (Zyprexa) can cause serious side effects including sedation, confusion, and sometimes Parkinsonian-like symptoms. Studies have shown that both atypical and older antipsychotics are associated with increased risk of death in elderly dementia patients. These drugs should not be used routinely, and if needed, the minimum dosage should be used for the minimum amount of time, under careful supervision of an experienced clinician.

Patients and caregivers should also be cautious of over-the-counter medicines containing diphenhydramine (Benadryl). Diphenhydramine is an antihistamine that tends to make people drowsy. It also has anticholinergic effects that may result in confusion and worsening cognition. Diphenhydramine is found in sleep aids such as Compoz, Nytol, Sominex, Unisom, and also in "night time" or "pm" version of popular pain relievers and cold and sinus remedies.

In essence, patients with Alzheimer's disease are particularly vulnerable to side effects from various medications. It is best to consult with your doctors and pharmacists to learn about the benefits and potential adverse effects of any new treatment therapy, including seemingly benign over the counter remedies<sup>2</sup>.

Several medications are approved by the U.S. Food and Drug Administration to treat symptoms of Alzheimer's. Donepezil (Aricept®), rivastigmine (Exelon®), and galantamine (Razadyne®) are used to treat mild to moderate Alzheimer's (donepezil can be used for severe Alzheimer's as well). Memantine (Namenda®) is used to treat moderate to severe Alzheimer's. These drugs work by regulating neurotransmitters, the brain chemicals that transmit messages between neurons. These drugs may help delay or prevent symptoms (thinking, memory, and communication skills) from becoming worse for a limited time and may help control some behavioral symptoms; however these drugs don't change the underlying disease process. They are effective for some but not all people and may help only for a limited time.

Doctors usually start patients at low drug doses and gradually increase the dosage based on how well a patient tolerates the drug. There is some evidence that certain patients may benefit from

higher doses of the cholinesterase inhibitors. However, the higher the dose, the more likely are side effects. Patients should be monitored when a drug is started. Report any unusual symptoms to the prescribing doctor right away. It is important to follow the doctor's instructions when taking any medication, including vitamins and herbal supplements. Also, let the doctor know before adding or changing any medications.

Alzheimer's disease research has developed to a point where scientists can look beyond treating symptoms to think about addressing underlying disease processes. In ongoing clinical trials, scientists are developing and testing several possible interventions, including immunization therapy, drug therapies, cognitive training, physical activity, and treatments used for cardiovascular disease and diabetes. Researchers hope to develop therapies targeting specific genetic, molecular, and cellular mechanisms so that the actual underlying cause of the disease can be stopped or prevented.

## Support for Families and Caregivers

Caring for a person with Alzheimer's disease can have high physical, emotional, and financial costs. The demands of day-to-day care, changes in family roles, and decisions about placement in a care facility can be difficult. Becoming well-informed about the disease is important. Alzheimer's San Diego can help teach families about the various stages of dementia and ways to navigate challenging behaviors and communication techniques. Good coping skills, a strong support network, and respite care are other ways that help caregivers handle the stress of caring for a loved one with Alzheimer's disease.

### Helpful videos on this topic:

Teepa Snow, Brain Changes, Dementia 101	<a href="http://www.teepasnow.com/resources/teepa-tips-videos">www.teepasnow.com/resources/teepa-tips-videos</a>
Teepa Snow, Understanding the Changing Senses – sight, sound, touch and smell	<a href="http://www.youtube.com/watch?v=j9FFLaymycg">www.youtube.com/watch?v=j9FFLaymycg</a>
Teepa Snow, Understanding Taste	<a href="http://www.youtube.com/watch?v=EqKnL7V8B0M">www.youtube.com/watch?v=EqKnL7V8B0M</a>
Teepa Snow, Vision Changes	<a href="http://www.youtube.com/watch?v=iaUsRa5kNyw">www.youtube.com/watch?v=iaUsRa5kNyw</a>
Teepa Snow, Understanding Apathy and Depression	<a href="http://www.youtube.com/watch?v=bvXKH6UoROs">www.youtube.com/watch?v=bvXKH6UoROs</a>

<sup>1</sup>Adapted from the National Institutes of Health Alzheimer's Disease Education and Referral Center, 9/19/16.

<sup>2</sup>Medications to avoid for patients. (2015, October 19). Retrieved January 20, 2017, from <https://www.mind.uci.edu/alzheimers-disease/articles-of-interest/medications-to-avoid-for-patients/>