



Alzheimer's Disease

EARLY DETECTION AND TREATMENT ARE CRITICAL TO SLOWING ITS PROGRESS

CONCETTA FORCHETTI, MD, PhD

Although public awareness of Alzheimer's disease has grown significantly in recent years, considerable confusion still exists about the disease, its symptoms and its relationship to dementia.

The confusion is not limited to the general public: Even physicians sometimes lack a clear understanding of Alzheimer's. In the past, when seniors exhibited signs of memory loss, mood changes and/or a diminished ability to perform everyday tasks, it was thought to be part of the normal aging process. Such symptoms were chalked up to natural changes in an aging brain — a process that doctors in those days called “organic brain syndrome.” Nonmedical types used a simpler term: senility.

Today, neuroscience has advanced to a point where we know “organic brain syndrome” is a meaningless term. We understand that aging brains are as unique and nuanced as the individuals whose thoughts, emotions, words and actions they control. We understand that Alzheimer's is the primary — but not the only — cause of dementia. We have tools that can help us distinguish between Alzheimer's and normal symptoms of an aging brain. And, although no cure exists for Alzheimer's, we have medications that can slow its progress, and we are conducting long-term clinical trials of other treatments that are fueling hopes of someday stopping the disease.

ALZHEIMER'S AND DEMENTIA

Much of the confusion about Alzheimer's stems from the erroneous belief that Alzheimer's and dementia are different. There also is a common

misperception that dementia is not as bad as Alzheimer's. Many of the people I have treated for Alzheimer's clearly have wanted to hear that they had dementia and not Alzheimer's.

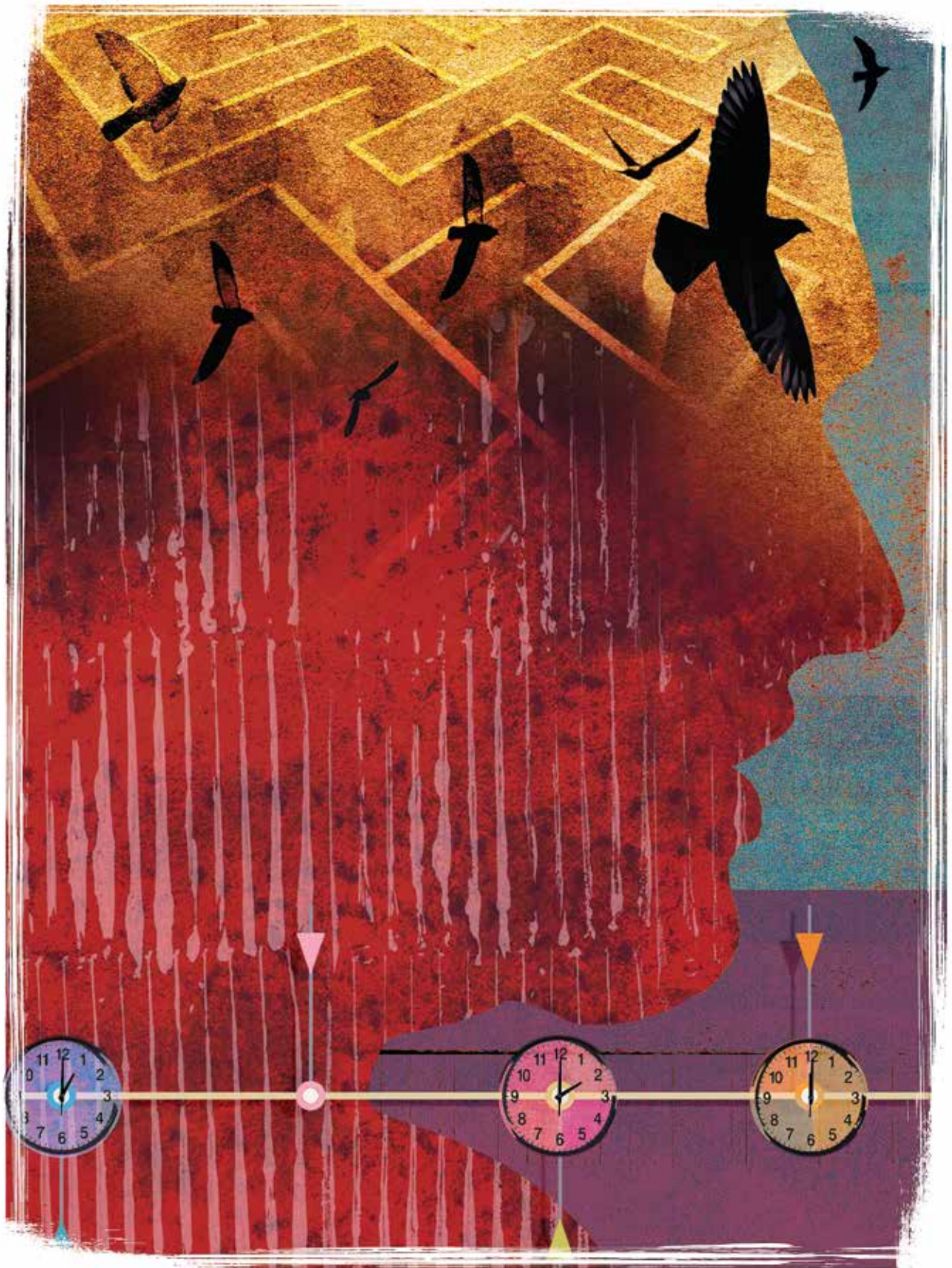
The facts are:

- Dementia is an umbrella term for brain dysfunction caused by different disease processes — just as heart failure is an umbrella term for the heart failing to pump blood properly, a condition that can be caused by arrhythmias, cardiomyopathy and many other factors.

- Alzheimer's is a disease process that causes dementia. Alzheimer's is the most common cause of dementia in people 65 and older, accounting for about 80 percent of all dementia cases in this population.

Strokes and mini-strokes are the second most common cause of dementia. They can destroy different areas of the brain, especially when they occur repetitively, causing what's known as vascular dementia. Other less common but still impor-

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tant-to-recognize causes of dementia include a neurodegenerative disorder in which Lewy bodies (abnormal deposits of the protein alpha-synuclein) accumulate in brain cells, causing diffuse Lewy body dementia, and a diverse group of disorders that deplete brain cells primarily in the frontal and temporal lobes, causing frontotemporal dementia.

TYPES OF ALZHEIMER'S

There are two types of Alzheimer's: early onset Alzheimer's disease, also known as familial Alzheimer's disease, and late onset Alzheimer's disease.

Familial Alzheimer's is a relatively rare disease that is passed genetically from parents to children in certain families. There are very few such families, and they are well known to geneticists and neuroscientists. Individuals in these families have a 50-50 chance of inheriting one of the three genes that cause familial Alzheimer's disease. If

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they have one of the genes, the disease usually manifests itself when they are in their late 30s or early 40s. It progresses rapidly, causing death by 50 or 55.

I have several such families in my population of Alzheimer's patients, and my team and I recommend genetic counseling for all members of these families so they can decide whether to undergo testing to determine whether they have inherited a familial Alzheimer's disease gene.

As our understanding of familial Alzheimer's genetics has grown, we have learned more about the proteins associated with each of the three genes, including how these proteins function in the brain and what happens to the brain when they stop functioning correctly. This knowledge has opened a window on the pathology and biochemical causes of the cascade of events that ultimately causes Alzheimer's, allowing us to better understand the basic science of the disease and to develop treatments that are more effective.

Symptoms of late onset Alzheimer's usually manifest themselves after people are 55 or 60, with

most cases surfacing when people are in their 70s. This form of the disease progresses very slowly, typically taking 20 to 30 years to run its course. Because it starts later in life and takes so long to progress, people with late onset Alzheimer's commonly die of other causes before the disease kills them.

For this reason, people diagnosed with this type of Alzheimer's should not think their life is over. The reality for many is far different: I have diagnosed many people with late onset Alzheimer's who continued to live very good lives for many years and eventually died of other causes.

WHAT CHANGES ARE NORMAL?

As with so many diseases, early diagnosis is critical to slowing the march of late onset Alzheimer's. But how can you tell when it's time to find out whether you or a loved one might have it? What are symptoms of normal brain changes due to aging? And what are symptoms of Alzheimer's?

Epidemiological studies of people between 50 and 80 have helped us answer such questions. These studies tell us that as we grow older, we should expect our brains to function more slowly and less efficiently. It might take you a little longer to memorize a phone number or other information.

You might find yourself getting overwhelmed by having to handle two or three tasks at the same time. You occasionally might misplace your purse, your wallet, your car keys, but you easily retrieve the item later. These are normal signs of an aging brain.

Initial symptoms of Alzheimer's typically involve recurrent forgetfulness — not of the distant past, but of the very recent past: Returning to the grocery store to buy an item you forgot you bought yesterday. Forgetting appointments. Forgetting to pay a bill because you forgot where you put it. Forgetting to take medications or taking them more often than you should because you forgot whether you took them the first time. This type of forgetfulness often is accompanied by mood swings — irritability, apathy, depression, anxiety — that reflect the frustration of cognitive decline.

When these symptoms start to appear frequently, interfering with a person's ability to perform daily functions successfully and safely, it is a sign that something beyond normal aging of

the brain is happening, and Alzheimer's testing is recommended.

GETTING TESTED

Alzheimer's testing is safe and standardized. Any well-qualified memory disorders center can assess someone for the disease. The testing process begins with an interview during which an individual or a loved one describes the individual's behaviors or symptoms. The individual then undergoes a physical and neurological exam and provides a blood sample for testing. Blood tests can reveal thyroid problems and other underlying conditions with symptoms that can mimic dementia.

The next step in testing is a brain scan — preferably an MRI. Today's MRI technology enables us to visualize memory centers in the brain. We can see whether they look normal or have been damaged or diminished in size by strokes or other disorders that can cause dementia.

The final stage of Alzheimer's testing is neuropsychological testing, the gold standard for measuring brain functions. I use it for all patients seeking a diagnosis — even those who can pass short, simple cognitive tests such as the Mini-Mental State Examination and the Montreal Cog-

People who are in denial about dementia — either their own or a loved one's — can pose a safety risk to themselves and to others.

nitive Assessment. Those tests can be very useful, but they can fail to identify the very early stages of Alzheimer's. Neuropsychological testing, which takes about three hours, is much more in-depth and provides much more precise measurements of an individual's ability to retain new information, solve problems and multitask.

The testing requires an individual to perform a series of relatively simple tasks. To test a person's memory, for example, a psychologist slowly reads a set of 12 to 16 words several times, asking the person at the end of each reading to name all the words he or she can remember. The psychologist counts the number of words the person remembers each time, and the numbers are used to plot a learning curve. After as many as five sets, the subject takes a 15- to 20-minute break, and then

the test resumes, with the psychologist asking the subject how many words he or she can remember. If the learning curve and the delayed recall are below the normal expected range for the subject's age, gender and education level, it is an indication of declining memory function. This result, combined with other abnormal findings, is used to determine a clinical diagnosis of Alzheimer's.

Another sign that raises suspicion of cognitive decline: If a person begins neuropsychological testing, stops abruptly, refuses to continue and never returns. Although the testing is lengthy, it is not hard to perform for people whose brains are functioning normally. When a person opts out of such testing, it's a sign that the person recognizes he or she cannot perform simple tasks, feels threatened and is afraid of learning the truth.

MOVING PAST DENIAL

People who are in denial about dementia — either their own or a loved one's — can pose a safety risk to themselves and to others.

Individuals in denial about their own dementia can experience a decline in their ability to live independently. Aside from the frustration of forgetting where they have left things, their dementia can lead to hazardous situations, such as driving a car when they no longer should, failing to turn off a gas burner in the kitchen or wandering away from home and getting lost.

Family members who recognize a loved one's cognitive decline yet fail to take action are shirking a serious responsibility, because their inaction can result in injury or death for their loved one or others. I have seen this happen, and it is tragic. If you think a loved one has Alzheimer's, it is imperative that you move past denial and seek help as soon as possible.

At the AMITA Health Memory Disorders Center in Chicago we work with families whose loved ones are in denial about their dementia to find ways to persuade them to undergo testing and to accept treatment. We also require patients diagnosed with Alzheimer's at an early stage to undergo a regularly scheduled, structured evaluation of their driving skills, with the understanding that if they fail the evaluation, they must surrender their driver's license and car keys.

It's important to lay this groundwork with the patient and his or her family early in the disease's



progression, when the patient still can understand the risks of driving and the idea that a day is coming when he or she no longer will be able to drive safely. Alzheimer's patients involved in accidents usually have advanced dementia, and the longer it takes to diagnose their condition, the harder it is to help a patient understand the risks and to avoid a tragic accident.

As the population ages, police departments are becoming more attuned to driving hazards presented by people with Alzheimer's. If they stop a senior for driving erratically, see that the driver is confused, and determine alcohol is not the cause, a growing number of police officers are suggesting to such drivers that they stop driving and consult with their physician about their driving problems.

To borrow a phrase from Hillary Clinton, it takes a village to care for people with Alzheimer's, and everyone needs to be aware of the risks presented by the disease.

RESEARCH ADVANCES

Safety is not the only reason for pursuing testing and treatment for suspected Alzheimer's as soon as its initial symptoms become apparent.

An early diagnosis of late onset Alzheimer's allows patients and their families to make plans, to prepare for the future and to enjoy life as much as possible, recognizing that the disease's course is a long one.

They also can take advantage of generic medications such as donepezil, rivastigmine and memantine, which have been shown to slow Alzheimer's progress. The earlier a patient can start on these medications, the more effective they can be.

To address the mood swings that often accompany dementia, these medications can be prescribed in combination with drugs known as selective serotonin reuptake inhibitors (SSRIs), which are commonly used to treat depression and anxiety. Treating mood swings is vital to improving the quality of life for Alzheimer's patients and their families, and physicians can prescribe specific SSRIs to address specific symptoms.

Advances in genetic testing for late onset Alzheimer's have improved the chances of identifying the disease in its earliest stages. Research has

shown that people with a gene known as ApoE4 have a greater risk of Alzheimer's, although some people with the gene don't develop the disease and some people without the gene do.

Those who test positive for ApoE4 can undergo a PET scan or a lumbar puncture and spinal fluid analysis to determine if two hallmarks of Alzheimer's — the proteins amyloid and tau — are present

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in their brains. With this testing, an individual can determine if they have these biomarkers decades before any Alzheimer's symptoms appear.

Amyloid deposits form plaque that builds up between nerve cells in the brain, while tau deposits form tangles, or twisted fibers of the protein, inside brain cells. Together, amyloid and tau contribute to the death of brain cells, which is the basic cause of Alzheimer's. Most people develop plaque and tangles as they age, but these biomarkers usually are more abundant in people with Alzheimer's, appearing first in the brain's memory and learning centers before advancing to other areas.

In recent years, a number of drugs have been developed to remove amyloid and tau from the brain and impede the disease's progress, but clinical trials in which people with moderate Alzheimer's have taken these drugs have produced poor results. Similar medications now are being tested in long-term clinical trials focused on people who have few or no symptoms of the disease but have tested positive for ApoE4, amyloid and/or tau.

AVOIDING ALZHEIMER'S

What can healthy people do to delay the onset of Alzheimer's or possibly prevent the disease? Studies have shown there is no silver bullet, but there are recommendations I give to children of patients with Alzheimer's: Control your weight, exercise, do not abuse alcohol or drugs, socialize frequently, get your sleep and exercise your brain

by working to learn something new every day. Research indicates these steps can be impactful, delaying the onset of Alzheimer's by several years in people at risk of developing the disease.

Right now, pursuing a healthy lifestyle is the best defense we have against Alzheimer's, and acting quickly to get tested and treated is the best way to slow its progress when symptoms appear.

Intervening early, before amyloid and tau can cause significant brain damage, is the focus of today's leading-edge clinical trials — and our best hope for scoring a significant victory against Alzheimer's. Time will tell, but I believe we are getting closer to a cure. Thanks to technological and pharmaceutical advances, we have gained

considerable ground in the last five years, and I remain hopeful that someday we will conquer this intractable disease.

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