

PART I

Preventing Alzheimer's

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Alzheimer's Disease

A lot of senior citizens in Sun City, Arizona, panic when they forget where they put their glasses or can't remember the name of someone they met at a cocktail party. Many middle-aged professionals, in the prime of their lives, worry as well. Naturally, one's first thought is Alzheimer's. How can you tell if this type of memory loss is the kind that is entirely natural and expected with age or the first sign of the onset of Alzheimer's, which is truly an illness? First, you have to know what Alzheimer's is and what it is not.

A Definition

Alzheimer's disease causes gradual memory loss, a decline in the ability to perform routine tasks, disorientation, difficulty in learning, loss of language skills, impairment of judgment, and personality changes. As the disease progresses, people with Alzheimer's become unable to care for themselves, and their loss of brain function eventually leads to the failure of other systems in the body, causing death three to twenty years from the onset of symptoms.

More simply, Alzheimer's is a brain disease. It is *not* normal aging. It affects cognitive function in multiple areas of the brain. As the life span in the United States and other industrialized nations continues to increase, Alzheimer's disease has emerged as one of the most common brain disorders. It looms large not only because it is becoming increasingly common or prevalent, but also because of its terrifying course. What begins as benign forgetfulness ends by ultimately ravaging the entire mind.

It is useful to keep in mind that Alzheimer's disease is a relative newcomer among the known degenerative brain diseases. In 1906, the German pathologist and neurologist Alois Alzheimer described a fifty-seven-year-old woman, Auguste D., who manifested progressive dementia (the inability to engage lucidly with other people and the loss of ability to conduct daily life), hallucinations (seeing or hearing things that are not there), and delusions (a false belief that things are occurring that are not). After Auguste D. passed away, Alzheimer succeeded in taking sections of her brain and putting stains on them so that he could identify the typical features of brain tissue, as well as the atypical. He observed what he called *amyloid plaques* (clumps of dark protein in the cortex and the hippocampus that may be seen by looking at the diseased brain through a microscope), and he described densely twisted bundles of *fibrils* (very fine fibers) that he called *neurofibrillary tangles*. I'll discuss these phenomena more later on.

Despite the fact that Alzheimer noted the signature signs of the disease in 1906, medical research in the disease lay dormant for nearly eighty years. Physicians treating the elderly accepted cognitive decline as a normal manifestation of the aging process partly because they lacked the appropriate research tools to properly understand it and to imagine a course of treatment. But in the late 1960s, Dr. Robert Katzman, a neurologist at Albert Einstein University and University of California–San Diego and one of my mentors, identified Alzheimer's as a potentially important and common disease. During the time that Dr. Katzman made this observation, many people did not recognize Alzheimer's disease and used terms like “hardening of the arteries” and “dementia.” Almost all of those cases have turned out to be Alzheimer's disease.

This makes it likely that this disease is not new, only the recognition of it is relatively so.

But the changes that an Alzheimer's-affected brain undergoes were not understood until 1984, when Dr. George Glenner and Dr. C. W. Wong of the University of California–San Diego established that the appearance of amyloid plaque or the existence of a protein called *amyloid beta peptide* was the core constituent of a brain showing signs of Alzheimer's. These are described in detail in chapter 2. This finding was the foundation of many of the discoveries about Alzheimer's that have occurred in the last twenty years, providing further avenues of research among molecular biologists, geneticists, and brain pathologists. This was the real beginning of meaningful discussions about treatment of Alzheimer's disease and even, perhaps, its prevention.

Molecular biologists found that the amyloid protein came from a parent molecule called an *amyloid precursor protein* (APP). Their discovery of mutations of APP led to the initial understanding that such molecular changes trigger Alzheimer's disease. The first solid indication that these mutations were culprits came from research by a team headed by Henry Wisniewski in 1985. They found that people with Down syndrome, a genetic condition, have a high risk of acquiring early-onset Alzheimer's disease, beginning in their forties, and that Alzheimer's is a virtual certainty in Down syndrome individuals who live to their fifties. Using other breakthroughs in genetic engineering, scientists soon were able to develop mice with mutations that caused them to get Alzheimer's disease. Now, there is a whole subfield in Alzheimer's research devoted to understanding the mechanisms by which the brain produces amyloid, the cellular biology of amyloid processing, and the main reasons it causes toxic events, cell damage, and subsequent brain damage.

Now that you know the basics and the history of research relating to Alzheimer's, here are some of the things we doctors look for when we suspect Alzheimer's disease.

Alzheimer's patients go through three phases as they progress from mildly affected to advanced dementia. These phases are summarized in the following list.

Common Clinical Features of Alzheimer's Disease by Stage

Early stage. This is also called mild Alzheimer's. This stage of the disease is often mistaken for old age. The patient and the family will frequently dismiss the symptoms, attribute them to other reasons (for example, stress, preoccupation, old age, and so on), or not take the signs and symptoms seriously. Later, I will discuss more specifically the key things to look for if you think someone you know may be starting to manifest symptoms of Alzheimer's.

- **Memory**

Poor recall of new information. People with Alzheimer's forget new facts and occurrences quickly, due to a loss of short-term memory. That is why they often repeat themselves. Long-term memory, or recall of things that happened in the distant past, is preserved.

- **Language**

Dysnomia (impaired naming of objects). People with Alzheimer's have trouble recalling words and names, even ones very familiar to them, to a far greater degree than those who experience normal aging.

Mild loss of fluency (language production). People with Alzheimer's tend to talk less over time.

- **Visuospatial**

Misplacing objects. People with Alzheimer's lose glasses, keys, and other objects very frequently or put them in unusual, even inappropriate, places.

Difficulty driving. People with Alzheimer's tend to have difficulty in perception and will make poor decisions while driving. This is a contentious issue that is often difficult for the family and the treating physician to deal with.

- **Behavioral**

Depression. People with Alzheimer's are frequently depressed and withdrawn. Often early signs of Alzheimer's, such as loss of interest in activities or loss of initiative, are

mistaken for depression. However, when the depression is treated, cognitive impairment remains in people with this disease.

Anxiety. People with Alzheimer's often experience anxiety, sometimes related to short-term memory loss. They tend to feel uncertain in situations that are not routine or familiar.

Intermediate stage. This also referred to as moderate Alzheimer's. Symptoms become very apparent as Alzheimer's progresses. Often, this is the stage when family members seek care for their loved one with Alzheimer's, frequently because the symptoms have spread beyond simple memory loss and are starting to take a toll on all family members involved in the care of the person.

Memory

Remote memory. People with intermediate Alzheimer's begin to forget things in the distant past or to confuse the past with the present.

Language

Nonfluent (meaning loss of ability to produce language). Patients experience progressive and overt loss of language production.

Poor comprehension. Over time, Alzheimer's patients lose their ability to understand or follow conversations and instructions.

Visuospatial

Getting lost. Alzheimer's patients may begin to get lost in stores or places they have been many times before or even in their own neighborhood. They have a decreased sense of direction.

Behavioral

Delusions. People suffering Alzheimer's may begin to believe things that have not occurred have taken place, or vice versa. Examples of delusions include thinking something was stolen, when the Alzheimer's patient has simply lost the object. Another example is the delusion that people are conspiring to put the Alzheimer's person away

or take his or her money. Yet another, more disturbing delusion is the idea that the spouse or caregiver is an impostor.

Depression. Alzheimer's patients often lose interest in participating in activities they once enjoyed. This can be either from the dementia or from depression. Sometimes it is difficult to tell. Alzheimer's patients tend to have less energy. This is frequently interpreted as depression.

Agitation. Verbal outbursts or physical threats for seemingly minor activities or requests such as bathing and eating. Often, patients become resistive to routine activities and may strike out at caregivers over seemingly minor things.

Sleep. Sleep disturbances are common complications of Alzheimer's disease progression and may include the loss of internal regulation of sleep, excessive medication use, sleep-disordered breathing, depression, and chronic bed rest. Related sleep disturbances like nocturnal wandering can increase caregiver burden.

Neurological

Frontal release signs. When Alzheimer's subjects are examined, they have features similar to infants such as a grasp reflex (a reflexive grabbing when something is placed in the palm) and a snout reflex (puckering of the lips in anticipation of being fed).

Extrapyramidal signs. Parkinson's disease-like features (stiffness, slowness of movement) may emerge at this stage, although they tend to be more pronounced in the advanced stage of the disease. When they are overt, we consider the possibility of other kinds of dementia.

Nonspecific gait disorder. People with Alzheimer's start to walk slower and may need assistance in walking.

Late stage. This is often referred to as severe Alzheimer's. By this stage, the disease has been present for many years, and most people with Alzheimer's disease are already in long-term care.

This is perhaps the most heartbreaking stage because at this point the people are dependent on others for care and survival. They lose their recognition of loved ones, even spouses of decades. They lose their ability to express their needs.

Memory

Short-term and long-term memories. Both are severely impacted. At this stage, people with Alzheimer's may no longer recognize loved ones or remember large segments of their lives.

Language

Lost language production. Patients with late-stage Alzheimer's often have lost language production to the point where their speech becomes largely unintelligible and their needs cannot be expressed clearly.

Behavioral

Agitation. Patients with Alzheimer's frequently become agitated. This might include physical aggression toward caregivers as well as resistance toward basic activities such as bathing and dressing.

Wandering. Patients with Alzheimer's frequently wander in the home or when unsupervised can wander in the neighborhood or even farther away.

Loss of insight. Late-stage Alzheimer's patients have no recognition or insight that there is anything wrong. When asked if they have Alzheimer's, they reply that they do not. This can be very distressing for families, especially when they try to point out a memory problem or an error in judgment; the person with Alzheimer's will flatly deny that anything is wrong. Because people with Alzheimer's lose insight, they can get agitated or paranoid as they are reacting to how people react to them, not understanding why other people react to them in certain ways.

Neurological

Incontinence. As Alzheimer's patients become very advanced, they lose control of bladder and bowel function.

This is one of the reasons people are placed into long-term care.

Frontal release signs. Infantile reflexes such as grasp, which are shed by the brain during normal childhood development, return with late-stage Alzheimer's.

Rigidity. Alzheimer's patients become increasingly slower and stiffer in movement.

Loss of gait. In the advanced stages, people with Alzheimer's are no longer able to walk and eventually cannot sit or hold themselves up.

Feeding and swallowing difficulties. In this stage, people forget to eat, forget to swallow, forget to chew, and pocket food (leave it in the mouth). The swallowing reflex becomes compromised, resulting in choking episodes and possibly pneumonia.

CASE STUDY

Anna Repeats Herself

Anna, an eighty-one-year-old woman, was brought to see me in my clinic at Sun Health Research Institute for an evaluation of memory loss of a progressive nature. The symptoms had been present for five years and were getting worse. Her memory loss originally took the form of a tendency to repeat questions and ideas. As the symptoms progressed, her daughter, Sylvia, reported that her mother was having trouble reasoning and was disoriented with regard to time, day, date, month, and year. Frequently, Anna did not understand where she was when outside the home. Sylvia described Anna as still experiencing anxiety and depression, which signified a personality change in her mother despite multiple courses of medication for depression. Anna now also tended to be verbally aggressive toward others, which was not her usual manner. In addition, Sylvia reported that her mother had begun to require supervision in dressing, bathing, and

grooming—what we physicians call “functional decline”—and required reminders to change her clothes. Frequently, Anna would wear the same clothes repeatedly. In addition, she had become socially withdrawn.

During my evaluation, Anna told me that she cooked and cleaned her house, and how her husband didn't care, repeating the same statement eight times. She was also very upset when I examined her, because she did not comprehend why she was there. Throughout the visit, she had obvious difficulty finding words. Even without any other medical or neurological evaluations, all these indications made it obvious that she had classic Alzheimer's disease in the late mild/early moderate stage.

The simple fact is that not all forgetfulness is Alzheimer's. Additionally, with a lot of myths surrounding Alzheimer's disease, it is good to start with basic facts about what is true and not true about Alzheimer's disease specifically, and memory loss in general.

Alzheimer's Myths and Truths

Myth: All forgetfulness is Alzheimer's.

Not true: Some mild forgetfulness for names is expected as we age. Forgetfulness that portends Alzheimer's is characterized by rapid forgetting of present-day information or thoughts, such as forgetting appointments or repeating questions and statements.

Myth: All Alzheimer's includes forgetfulness.

True: One of the most salient features of Alzheimer's is short-term memory loss in the context of impairment in other aspects of living.

Myth: Alzheimer's is just old age.

Not true: Alzheimer's is a disease like heart disease, cancer, diabetes, and stroke, and can strike people as young as their forties or fifties while never affecting others of advanced age.

Myth: Dementia and Alzheimer's are the same thing.

Partially true: Alzheimer's is a type of dementia. So all Alzheimer's is dementia, but not every dementia is Alzheimer's.

Myth: I can't get Alzheimer's because it does not run in my family.

Not true: A family history of Alzheimer's certainly increases the risk but is not absolutely necessary to get Alzheimer's.

Myth: Memory loss can only occur from degenerative brain diseases.

Not true: There are medications that can cause or compound memory loss. Some metabolic conditions such as low blood sugar or low sodium can also exacerbate or mimic memory loss.

Myth: Alzheimer's disease can be diagnosed only at autopsy.

Partially true: This common myth is based on scientific opinions and criteria that are over twenty-two years old. Our science has progressed significantly since then; under the right circumstances, some doctors can diagnose Alzheimer's with greater than 90 percent accuracy during life. Thus, we are beginning to approach diagnosis not simply by excluding other conditions that can cause memory loss but by specifically identifying Alzheimer's with reasonably high accuracy. This is discussed further in chapter 19.

Not All Dementia Is Alzheimer's

Dementia is a category of disease. Saying a person has dementia is much like saying a person has cancer. Well, what kind of cancer? One could have leukemia, lymphoma, sarcoma, carcinoma, or melanoma, for example. Likewise, there are many types of dementia.

All dementias are characterized by cognitive decline (such as memory, orientation, and executive function [planning and executing tasks]) that affects daily life, but each type of dementia has different features that distinguish one kind from another. These

differences are important, since they each require different diagnoses and treatment plans. These are summarized in the following list.

Types of Dementia

- **Alzheimer's disease.** Described earlier. It accounts for only half to two-thirds of all dementias. The remaining third includes the ones listed below.
- **Dementia with Lewy bodies (DLB).** This is the second most common type of dementia. It is characterized by progressive dementia coupled with slowness of movements and Parkinson's-like features (stiffness and problems walking), as well as clearly described hallucinations (particularly visual hallucinations: a tendency to see things that are not there and responding to stimuli from the person's own mind). People with DLB tend to have very rapidly progressing dementia and fluctuations of clarity followed by confusion. They tend to be very sensitive to medication that, although intended to improve symptoms, can make these sufferers worse. Interestingly, they may have a tendency to act out dreams that may precede the onset of the dementia. *Lewy bodies*, first identified by Frederic Lewy, are particular changes seen in brain cells and are most commonly associated with Parkinson's disease. What distinguishes DLB from Parkinson's is that Lewy bodies are concentrated in one part of the brain in Parkinson's, but widely distributed in DLB. Most sufferers of DLB have autopsy findings consistent with Alzheimer's disease.
- **Vascular dementia.** Strokes (cerebral thrombosis, hemorrhage, or cerebral embolism) can cause dementia, and such memory loss and cognitive decline can even start fairly abruptly following a stroke. *Vascular dementia* is characterized by changes identified on a brain scan such as a CT or an MRI. A clearly identified history of stroke is helpful although not always present. When examining a person with vascular dementia, an abnormal neurological examination is evident with focal weakness, loss of coordination, or trouble with

balance. This type of dementia may not progress and can even improve with the right type of treatment.

- **Alzheimer's mixed with vascular dementia.** At autopsy, most individuals with vascular dementia have enough biological changes in their brains to fulfill the pathological criteria for Alzheimer's. Pure vascular dementia is far less common than is the mixture between Alzheimer's and stroke-induced vascular dementia. With mixed vascular/Alzheimer's, people can become worse even when they have not had another stroke. Some scientists and researchers believe that the causes of vascular dementia and Alzheimer's overlap. This will be discussed in chapter 7.
- **Frontotemporal dementia (FTD), or Pick's disease.** This is a relatively uncommon type of dementia, named for Arnold Pick, with an earlier age-of-onset (forty to sixty-five years old) than Alzheimer's disease. Many FTDs are linked to genetic mutations on chromosome 17 (scientists call these "the tauopathies"). More recently, scientists have discovered new mutations in a gene called progranulin. Symptoms include prominent language changes such as *anomia* (inability to name an object), *aphasia* (inability to generate or comprehend language), *echolalia* (a tendency to repeat everything said to them), and *perseverative speech* (a tendency to repeat a word or phrase in an obsessive manner, not realizing that they are doing so). Many patients suffering from this type of dementia lose social skills and display inappropriate behavior and judgment and lack of insight.

One of my patients was a fifty-nine-year-old gentleman. His wife explained to me that he had started having trouble understanding what she was telling him about one to two years before their visiting my office. She also told me that he had tried to get out of the car when she was driving on the highway to their appointment with me. When I examined him, he was very restless and wandered about the room, standing and sitting repeatedly. Also during my examination of him, he could not converse well; he had trouble speaking as well as understanding. He had Pick's disease.

- **Parkinson's disease.** Parkinson's initially begins with movement problems and is clinically characterized by the presence of tremor (more commonly while the arms and legs are at rest and not in motion), *cogwheel rigidity* (stiff joints and limbs) and *bradykinesia* (slowness of movement). Parkinson's patients commonly have problems walking and have a tendency to fall. Dementia is common in advanced cases, although estimates of dementia prevalence vary widely—anywhere from 27 to 78 percent in some studies. Parkinson's dementia is different from Alzheimer's in that Parkinson's patients have slower recall, whereas Alzheimer's patients won't remember the same items at all. People with Parkinson's dementia tend to have more hallucinations. Both loss of mobility and loss of cognition contribute to the functional declines seen in Parkinson's dementia.
- **Huntington's disease.** This is a rare, inherited disease, detectable by genetic testing and brain scan, that has dramatic phenotypic characteristics, including *chorea* (uncontrollable writhing movements), depression, psychiatric changes, and dementia. Huntington's most commonly strikes individuals in their forties, fifties, and sixties, and has been genetically linked to mutations that occur on chromosome 4.
- **Other degenerative diseases.** Other diseases, such as progressive *supranuclear palsy*, a Parkinson's-like condition manifested by patients having significant balance problems and trouble moving their eyes; and *Lou Gehrig's disease* or *amyotrophic lateral sclerosis* (ALS), a degenerative disease that causes progressive atrophy (shrinkage) of muscles. Other degenerative brain diseases are associated with dementia. These are, for the most part, quite rare.
- **Dementias secondary to alcohol.** Alcohol-related dementia is well described and is linked to chronic consumption of alcohol for years. Keep in mind this is a distinct risk unrelated to mild alcohol use, which actually may protect against Alzheimer's disease. Alcohol-related dementias are subcategorized into different types. It is important to recognize, however, that acute confusion related to alcohol may also be due

to a vitamin B₁ (thiamine) deficiency. Without proper treatment, thiamine deficiency from alcohol consumption can lead to a type of dementia called *Korsakoff dementia*, which is characterized by severe *anterograde amnesia* (inability to gather new memory), and *confabulation* (making things up to fill the gaps in memory). See chapter 12 for more on Korsakoff's and alcohol-related dementias.

- **Depression/pseudodementia.** Depression can masquerade as dementia, particularly in younger people. Depression-induced pseudodementia is distinguished from degenerative dementia by the sufferer's apathetic demeanor at diagnosis. Moreover, when such a patient gets treatment, his or her memory improves, unlike an Alzheimer's patient with depression, who may not necessarily experience an improvement in memory.
- **Normal pressure hydrocephalus (NPH).** This is an increasingly recognized condition that typically affects elderly individuals. It is characterized by walking and balance problems, followed by trouble controlling bladder function and memory loss. Important in the diagnosis of NPH is identification of abnormally large spaces in the brain called the *ventricles*; due to overaccumulation and reduced clearance of *cerebrospinal fluid* (CSF). NPH comes with good news: it is actually a treatable condition, and under the right circumstances, sufferers can expect a full recovery. A shunt that drains fluid from into the abdomen is implanted surgically and can be programmed to increase or decrease flow or pressure as needed. These programmable shunts have meant vast improvements in NPH therapy and hope for patients of this dementia.
- **Structural lesions.** Although rare, brain tumors can become symptomatic in the form of dementia. Twice, I have seen brain tumors present as dementia. Typically, they are large, near the middle of the brain, and involve the frontal lobe (front part of the brain). In both circumstances, the tumor was removed and the patient improved.

- **Endocrine disorders (hypothyroidism).** Thyroid deficiency is a well-known cause of dementia. It is less common than it used to be, since thyroid levels are routinely checked in medical practice. When a person has cognitive decline and dementia from thyroid deficiency, he or she tends to have other symptoms of hypothyroidism as well, including low energy level and weight gain.
- **Metabolic disorders.** Low sodium and low blood sugar at critically low levels can cause acute confusion and coma but are not common causes of dementia. We routinely check for low electrolytes in the course of a dementia evaluation.
- **Infections (for example, neurosyphilis, AIDS, CJD).** Before 1929, the most common form of dementia in the world was from syphilis. Since that time, with the advent of penicillin, dementia from syphilis has become quite rare in the Western world. It is still sometimes seen in urban clinics and can be a presenting sign of syphilis but mostly would follow the presence of other symptoms such as genital changes and a rash on the palms and the feet. Diagnosis of neurosyphilis involves a spinal tap to detect the infection in the central nervous system.

Dementia from AIDS is a frequent disabling complication in advanced stages and is manifested by poor concentration and personality changes such as listlessness and indifference. *AIDS dementia complex*, as it is commonly called, affects the front part of the brain. It would not be a presenting feature of AIDS and occurs after AIDS symptoms have been present for long periods of time.

Creutzfeldt-Jakob disease, or CJD, is the human equivalent of mad cow disease. In cows, it is called *bovine spongiform encephalopathy*; in sheep, it is called *scrapie*. In humans, it is acquired from transplantation or ingestion of infected human or cow tissue. Symptoms take years from time of infection to manifest. More specifically, the symptoms of the disease may start twenty years or more after exposure to the infected source. It was originally described in cannibals from New

Guinea who ate human remains, out of cultural beliefs. It is not limited to cannibals, but it does require exposure to the infection. The cause of CJD is neither a virus nor bacteria but rather a viruslike protein called a *prion*. CJD is characterized by rapid dementia and *myoclonus* (involuntary jerking of the body). Changes in spinal fluid and brain-wave studies (EEGs) can confirm a diagnosis; mention CJD or mad cow, however, and fear is struck in the heart of health-care workers, because there are no effective treatments. Once symptoms start, CJD is uniformly fatal and life expectancy is less than one year. Thankfully, this is still quite rare, and infection from eating infected meat is not only exceedingly infrequent but still quite controversial as regards its being a definitive cause of this disease.

- **Medication effects.** Many medications, prescribed and over-the-counter alike, may adversely affect memory. These include preparations for sleep, such as anything that has “PM” in the name; some antihistamines for allergies, such as diphenhydramine (Benadryl and other brands); certain bladder medications, such as oxybutinin (Ditropan); and some epilepsy medications, such as phenobarbital. In fact, many drugs affect cognitive function when taken in excess, including such sedatives as diazepam (Valium). Ask your doctor if the medications you are taking could affect your memory.

How Do You Know You Are Getting Alzheimer's?

Toward the end of this book, in chapter 19, are a few questionnaires that you can take if you are concerned that you or a loved one is developing Alzheimer's. Early Alzheimer's is often mistaken for old age. Loved ones and friends often overlook the misplacing of keys as simple inattention. But if such events of memory loss become repetitive or obvious, consider seeking medical attention. It is important to think of Alzheimer's and dementia as you would any disease: you *need* to seek medical attention.

Beyond this awareness, the following telltale signs indicate that something is really wrong. These ten warning signs are also seen at the Alzheimer's Association Web site (www.alz.org).

Ten Warning Signs of Alzheimer's

- **Memory loss that affects job skills.** If you are laid off, keep moving from job to job, or are demoted because you cannot remember tasks or have trouble learning new tasks, you may be exhibiting signs of early Alzheimer's.

Once I had a patient who was a battleship repairman. He was a master craftsman who had to follow and understand very complex diagrams in order to repair battleships. His first sign of Alzheimer's was difficulty in reading diagrams and following instructions on complicated repair jobs. These problems and difficulties ultimately led to his losing his job.

Another patient of mine was an executive who noticed that she was having trouble understanding, tracking, and remembering her account spreadsheets and business plans. This change in her work habits alarmed her and forced her into retirement earlier than planned. These symptoms were her first sign of Alzheimer's.

Yet another of my patients was a nurse anesthetist and a faculty member of a nearby nursing school. She had an important job, being responsible for the nurse anesthesia program at that school. She ended up on disability because she lost her ability to develop curricula, teach, plan, and administer the very programs she had created. First, she was put on part-time work status and ultimately on disability. Her Alzheimer's was positively diagnosed at the age of fifty-nine.

- **Difficulty performing familiar tasks.** These can include cooking, check writing and other bookkeeping, supermarket shopping, and home maintenance. Simply put, if the person is struggling to do a familiar task or has given it up altogether, suspect Alzheimer's.

One of my patients had been a general contractor. He could build or repair anything in the home. His first sign that he had Alzheimer's was that he was starting a lot of

home-repair projects but either not finishing them or taking weeks to finish what in the past would have taken him mere hours or days to complete.

Another patient of mine used to be a great cook. She was admired and beloved by friends and family alike because of her culinary skills. Her first sign of Alzheimer's was her inability to follow recipes. Her husband reported that the taste of her cooking was not like it used to be.

Yet another of my patients used to be able to calculate his taxes by hand every year (I certainly can't do that). His Alzheimer's was signaled by his trouble following the line-by-line instructions and his loss of the ability to calculate his taxes with pencil and paper.

Another of my patients was formerly a music conductor and an avid musician. He could hear every instrument in his head when he conducted and would memorize entire musical scores. The onset of Alzheimer's caused him to lose the ability to read and follow the music sheets when he was conducting. Furthermore, he could no longer memorize an entire score.

The recurrent theme here is that all of these people were reported to have difficulty doing tasks they had done not only repeatedly but well in the past.

- **Problems with language, especially words and names.** This is a common complaint in Sun City and among seniors in general, so let me make a distinction here. If you have not seen someone you know for twenty years and you can't remember his/her name, that is merely a "senior moment." That kind of trouble remembering names probably does not represent the beginning Alzheimer's disease. However, when it is Alzheimer's disease, the word-finding difficulty can be much worse. Recently I saw a patient with Alzheimer's who called her spouse by her son's name.
- **Substituting one word for another.** This phenomenon is called *paraphasia*. In paraphasia, the concept is understood

but one word is substituted for another. For example, a person with Alzheimer's might refer to a wooden pencil as a pen. In descriptive paraphasia, the person describes the object in place of naming it. For instance, someone with descriptive paraphasia might call a watchband "the part that keeps it on the wrist." Both paraphasia and descriptive paraphasia are common in Alzheimer's. Often a caregiver is forced to play the guessing game to determine what the person with Alzheimer's is talking about or whom the individual is referring. For example, the woman I mentioned above called a "watch" a "clock" and called the tip of the pen "the ink." She made other mistakes of naming as well.

- **Disorientation to time and place.** This includes trouble tracking days and dates. In Sun City, many of my patients hide their deficit by saying, "Doc, I am retired—I don't have to know that." If the person is getting ready for church, however, thinking it is Sunday but it is Wednesday, then it is time to worry. Many of my patients suffering from Alzheimer's look at the newspaper or calendar daily to know what is the day, date, month, or year. Regularly I ask the year or other items of orientation. One gentleman replied 1947 for the year, when it was 2007.
- **Poor or decreased judgment.** Examples of decreased judgment might include a person's diminished ability to track investments, or trusting others to do it for him or her without knowing them well. This might manifest itself in an increased vulnerability to telemarketers, door-to-door solicitation, or giving away money without having a full accounting of the recipient's finances. When the dementia gets worse, often there is paranoia. People with Alzheimer's might believe that family members are conspiring to take their money away even when things are explained to them. They may become mistrustful of those who had been trustworthy.
- **Problems with abstract thinking.** People with Alzheimer's have trouble grasping abstract thoughts. This can include

learning new tasks or trouble comprehending nuanced topics such as poetry, metaphors, or difficult story lines in books and movies.

- **Misplacing things.** This is a manifestation of short-term memory loss. In normal aging, misplacing things is an infrequent event. With Alzheimer's disease, it can become so frequent to the point that families make looking for objects such as keys and glasses a part of their daily routine. One man I know spends all his daytime hours trying to find objects that his wife, my patient with Alzheimer's, misplaces.
- **Changes in mood or behavior.** Many people with Alzheimer's manifest depression and/or anxiety. This is often identified by loss of interest or by complaints of fatigue. Sometimes, normally social individuals will become socially withdrawn at the onset of clinical Alzheimer's.
- **Changes in personality.** Frequently, families comment about a senior's increased irritability and hostility toward loved ones. Mainly, they have a "shorter fuse." Alternatively, people with Alzheimer's may become passive, docile, or complacent.

Following is an example of personality change manifested as irritability and hostility:

Patient: "Dear, when is my appointment?"

Spouse: "I have told you five times already. It is tomorrow morning!"

Patient: "No, you haven't! You are lying. I would remember if you told me. . . ."

- **Loss of initiative.** Patients with Alzheimer's disease often lose interest in activities they formerly enjoyed, such as hobbies, reading, or chores, and prefer to become sedentary. Loss of initiative is often mistaken for depression.

If you recognize these signs in yourself or someone you know or love, then maybe it is time to see your doctor about it. Ultimately, it is important to recognize the symptoms and not ascribe them to old age or stress. What to do about Alzheimer's is discussed in more detail in chapter 19.

From Normal Aging to Alzheimer's: Mild Cognitive Impairment

People do not go from normal one day to Alzheimer's the next. The transition to Alzheimer's disease passes through an intermediate state called *mild cognitive impairment* (MCI). Metaphorically, MCI is the chest pain before the heart attack, the colon polyp before the colon cancer, the mole before the melanoma, the slightly elevated blood sugar before the diabetes. It is the intermediate state between being normal and having Alzheimer's.

MCI is characterized by subtle but measurable memory problems, and those who suffer from MCI have memory problems that are greater than typical for their age. Currently, this is a topic of intense debate in the medical community because many top researchers and clinicians believe that if intervention occurs at this intermediate stage, Alzheimer's disease might be delayed or arrested completely. Here are the clinical criteria for MCI:

- Memory difficulties are attested to by a patient and/or the patient's family. These lapses can interfere with the patient's ability to adapt and function in daily life.
- Selective memory lapses are measured by neuropsychological tests (extensive paper-and-pencil tests administered by trained professionals called *neuropsychologists*) while other brain functions register normal or near-normal.
- Although the patient's ability to complete complex tasks may be compromised, other activities of daily living, such as traveling, paying bills, and balancing a checkbook, remain unaffected.
- The patient is not demented. The distinguishing feature that separates MCI from Alzheimer's or dementia is the absence of functional impairment. Generally, such people are still getting along through life.

MCI is a common condition that may or may not be an omen of the decline in memory that accompanies the onset of Alzheimer's. Until very recently, doctors and scientists have not

had a consistent definition for this stage of impairment, making it difficult to estimate how common MCI really is. In long-term community-based studies of elderly subjects, we estimate that between 2 and 5 percent of people will convert from a cognitively normal state to dementia each year. Similarly, the incidence of cognitive impairment without dementia in these studies rises rapidly with age, reaching 2.4 to 7.9 percent by ages eighty to eighty-four. When we apply a strict definition to MCI with rigorous clinical and scientific criteria to back it up, then studies have reported the incidence of MCI to average around 1 percent per year. The time taken to “convert” from normal cognition to MCI and from MCI to dementia is the measurement that has been used to gauge the rate of cognitive change.

Although it's a crude measure of the progress of disease, this rate of conversion is also important because it helps us measure the efficacy of various drugs. In addition, it helps us predict the rate of the progress of the disease in a population that is converting to Alzheimer's in precipitous numbers. Further, as a transitional state between normal aging and Alzheimer's disease, it is a barometer of risk for developing Alzheimer's. Between 10 and 15 percent of all individuals diagnosed with MCI convert to Alzheimer's every year. In fact, there is a 50 percent conversion after five years and more than a 90 percent conversion after ten years.

In population-based epidemiological studies—that is, studies that are done on the general population rather than in a defined community—one-quarter of all MCI cases revert to a normal cognitive state, about half remain unchanged, and another quarter become demented within two years. In contrast, clinical studies of subjects with identified MCI with prominent memory loss are much more likely to convert to dementia, and reversals are rare. In fact, someone with MCI who has mainly memory loss is twenty-six times more likely to develop Alzheimer's than is an age-matched normal individual.

Although it is a very strong indicator, not all MCI is a prelude to Alzheimer's. Infrequently, MCI can be a marker of stress, depression, hearing loss, heart disease, nutritional deficiency, sleep

disturbance, or inactivity. I have seen sleep apnea that was so severe that it caused memory impairment. Once it was treated, memory loss drastically improved.

CASE STUDY

Old Age or MCI?

Heidi, an eighty-year-old woman with sixteen years of education, was referred to me for evaluation of memory loss. The patient articulately described her situation in her own words. She noted memory loss, such as a tendency to leave items cooking on the stove—she had burned many pans as a result. She said she had trouble remembering tasks, and forgot why she was doing things. She denied a tendency to repeat herself. She noted that she had become more withdrawn and been slightly depressed, indicating personality and mood changes. There was also a functional decline, as manifested by her admission to a tendency to procrastinate, which she never used to do. She got lost while driving and had a decreased sense of direction. When I examined her and tested her orientation, there was some disorientation to place. She also noted that she was having trouble finding words and names in conversations. She had not decreased her pursuit of pleasurable activities, however, and denied the presence of hallucinations or delusions. Her memory screening showed that she had difficulty recalling a name and address that I asked her to remember after a five-minute delay. The rest of her neurological exam was normal.

Further evaluation with extensive neuropsychological tests (the paper-and-pencil test described on page 32 and further in chapter 19) revealed a significant problem with memory but no problems in other areas tested. She therefore had MCI.

If MCI can present its symptoms so subtly, how can you tell if you have it or not? Diagnosing MCI is often challenging and is

best done with neuropsychological tests. These tests are paper-and-pencil memory tests that often take several hours to complete. Essentially, they are mental gymnastics.

One study from the University of California–Irvine found that using simple tests of memory (remembering a list of items) was 98 percent accurate in distinguishing MCI from early Alzheimer's, and 97 percent accurate in distinguishing normal memory for age from MCI. These rates show that getting tested is accurate and worthwhile. Anyone experiencing symptoms of MCI, whether it's you or someone you know, should seek an evaluation that includes blood tests and imaging.

Treating MCI is controversial, and experts have not reached a consensus that treatment with the medications available today is productive. Some physicians believe that the drugs used to treat Alzheimer's could be used to treat MCI. However, recent studies only show modest benefit with most Alzheimer's drugs currently on the market. Only donepezil (Aricept) has been shown to delay conversion to Alzheimer's and, even then, this is a delay of only six to twelve months, not a long-term preventative measure. With so little agreement in the medical community, the decision to treat MCI is one that should take place between the patient and a physician who has the most up-to-date knowledge about this condition.

Real MCI is the window a person has to address long-term life plans, like legal and financial matters, and family discussions about caretaking. Avoiding addressing the symptoms of MCI may result only in confronting a crisis situation later once the ravages of Alzheimer's have fully manifested themselves.

When Is It Old Age and When Is It Dementia?

Not all memory loss is Alzheimer's. Conversely, Alzheimer's is not simply old age. It is important to realize that most memory lapses in people over age fifty are likely benign. The term coined for benign forgetfulness is *age-associated memory impairment*.

Forgetting where you parked the car at the mall or your grandchild’s name may just be old age, but forgetting that you have been to the mall or forgetting that your grandchild is related to you is more serious. There is a difference. In the early stages, such lapses may be subtle, and the person can cover for these changes. However, every case of dementia reaches a point where it can no longer be confused with old age. The table below summarizes the difference between the two.

When Is Memory Loss Normal Aging and
When Is It Alzheimer’s?

ABILITY	NORMAL AGING	ALZHEIMER’S DEMENTIA
Independent activities of daily living (for example, driving, finances, telephone, shopping)	Preserved	Impaired early and worsens with disease progression
Personal-care activities of daily living (for example, dressing, grooming, bathing)	Preserved	Impaired as disease progresses
Language	Occasional word-finding difficulties	Frequent loss or misapplication of words
Complaints of memory loss	Frequent, particularly for words and names	Does not complain of memory loss
Awareness of memory loss	Preserved	Impaired
Social skills	Intact	Preserved early, lost later
Memory for recent events	Details preserved	Either recall is lost altogether or details are lost

(continued)

When Is Memory Loss Normal Aging and
When Is It Alzheimer's? *(continued)*

ABILITY	NORMAL AGING	ALZHEIMER'S DEMENTIA
Performance on cognitive testing	Preserved in all areas	Impaired in memory and other areas such as orientation, language, executive function
Orientation	Preserved, does not get lost, tracks days, dates, and time	Impaired; gets lost even in own neighborhood, has trouble with dates and time
Able to learn new skills	Slow but preserved	Lost. Cannot learn new technologies such as programming a remote control or operating a new appliance

Final Thoughts and Recommendations

- Know and pay attention to the telltale signs of memory loss.
- Alzheimer's is a disease; it is not simply old age.
- Alzheimer's is a type of dementia.
- Not all dementia is Alzheimer's.
- Don't ignore signs of cognitive decline; if they are apparent in you or someone you love, seek medical attention.