

Other Dementias

Dementia is the loss of cognitive functioning, which means the loss of the ability to think, remember, or reason, as well as behavioral abilities, to such an extent that it interferes with a person's daily life and activities. Signs and symptoms of dementia result when once-healthy neurons (nerve cells) in the brain stop working, lose connections with other brain cells, and die. While everyone loses some neurons as they age, people with dementia experience far greater loss.

Researchers are still trying to understand the underlying disease processes involved in the disorders. Scientists have some theories about mechanisms that may lead to different forms of dementias, but more research is needed to better understand if and how these mechanisms contribute to the development of dementia.

While dementia is more common with advanced age (as many as half of all people age 85 or older may have some form of dementia), it is not a normal part of aging. Many people live into their 90s and beyond. Memory loss, though common, is not the only sign of dementia. For a person to be considered to have dementia, he or she must meet the following criteria:

- Two or more core mental functions must be impaired. These functions include memory, language skills, visual perception, and the ability to focus and pay attention. These also include cognitive skills such as the ability to reason and solve problems.
- The loss of brain function is severe enough that a person cannot do normal, everyday activities

In addition, some people with dementia cannot control their emotions. Their personalities may change. They can have delusions, which are strong beliefs without proof, such as the idea that someone is stealing from them. They also may hallucinate, seeing or otherwise experiencing things that are not real.

Types of Dementia

- Alzheimer's disease
- Corticobasal degeneration
- Creutzfeldt-Jakob disease
- Frontotemporal disorders
- Huntington's disease
- Lewy Body dementia
- Mixed dementia
- Secondary dementia/chronic traumatic encephalopathy
- Vascular dementia

ALZHEIMER'S DISEASE

While the first symptoms of Alzheimer's disease vary from person to person, and the disease advances at different rates, experts have developed staging systems based on documented common patterns of symptom progression. These stages can provide general guidelines for understanding the progression of Alzheimer's symptoms and planning appropriate care:

3-Stage Alzheimer's Disease Model *(taken from www.nih.gov)*

- Stage 1 – Mild/Early Stage - As Alzheimer's disease progresses, people experience greater memory loss and other cognitive difficulties. Problems can include wandering and getting lost, trouble handling money and paying bills, repeating questions, taking longer to complete normal daily tasks, and personality and behavior changes. People are often diagnosed in this stage.
- Stage 2 – Moderate/Middle Stage - In this stage, damage occurs in areas of the brain that control language, reasoning, sensory processing, and conscious thought. Memory loss and confusion grow worse, and people begin to have problems recognizing family and friends. They may be unable to learn new things, carry out multistep tasks such as getting dressed appropriately, or cope with new situations. In addition, people at this stage may have hallucinations, delusions, and paranoia and may behave impulsively.
- Stage 3 – Severe/Late Stage - Ultimately, plaques and tangles spread throughout the brain, and brain tissue shrinks significantly. People with severe Alzheimer's cannot communicate and are completely dependent on others for their care. Near the end, the person may be in bed most or all of the time as the body shuts down.

CORTICOBASAL DEGENERATION (CBD)

CBD is a progressive neurological disorder characterized by nerve-cell loss and atrophy (shrinkage) of specific areas of the brain, including the cerebral cortex and the basal ganglia. The disorder tends to progress gradually, with the onset of early symptoms around age 60. At first, one side of the body is affected more than the other side, but as the disease progresses both sides become impaired. An individual may have difficulty using one hand, or one's hand may develop an abnormal position.

Other signs and symptoms may include memory loss; trouble making familiar, focused movements (apraxia) such as brushing one's teeth; involuntary muscular jerks (myoclonus) and involuntary muscle contractions (dystonia); alien limb, in which the person feels as though a limb is being controlled by a force other than oneself; muscle rigidity (resistance to imposed movement); postural instability; and difficulty swallowing (dysphagia). People with CBD also may have visual-spatial problems that make it difficult to interpret visual information, such as the distance between objects.

There is no cure for CBD. Supportive therapies are available to reduce the burden of certain symptoms. For example, botulinum toxin can help control muscle contractions. Speech therapy and physical therapy may help one learn how to cope with daily activities.

CREUTZFELDT-JAKOB DISEASE (CJD)

CJD is a rare brain disorder that affects about one in every million people worldwide each year, CJD belongs to a family of diseases known as the transmissible spongiform encephalopathies, or TSEs. Spongiform refers to the fact that the brain becomes filled with microscopic swellings that give the appearance of holes, like a sponge. CJD and other TSEs are believed to be caused by infectious proteins called prions that become misfolded. Scientists believe that the presence of misfolded prions can trigger normal proteins to misfold as well, causing a chain reaction. These abnormal prion proteins tend to clump together, which is believed to be related to the brain damage.

Symptoms usually begin after age 60, and most people die within a year of onset. In most cases, CJD occurs in people who have no known risk factors for the disease; however, an estimated 5 to 10 percent of cases in the U.S. are associated with genetic mutations. In addition, a type of CJD, called variant CJD (vCJD), has been found in Great Britain and several other European countries. vCJD has been observed to affect people who are younger than those with other forms of CJD and is believed to be caused by eating beef from cattle infected with a TSE called bovine spongiform encephalopathy, more commonly known as “mad cow disease.”

FRONTOTEMPORAL DISORDERS

In FTD, changes to nerve cells in the brain's frontal lobes affect the ability to reason and make decisions, prioritize and multitask, act appropriately, and control movement. Some people decline rapidly over 2 to 3 years, while others show only minimal changes for many years. People can live with frontotemporal disorders for 2 to 10 years, sometimes longer, but it is difficult to predict the time course for an affected individual.

In some cases, FTD is associated with progressive neuromuscular weakness otherwise known as amyotrophic lateral sclerosis (ALS, or Lou Gehrig's disease). The signs and symptoms may vary greatly among individuals as different parts of the brain are affected. No treatment that can cure or reverse FTD is currently available.

Behavioral variant (bvFTD) causes a person to undergo behavior and personality changes. People with this disorder may do impulsive things that are out of character, such as steal or be rude to others. They may engage in repetitive behavior (such as singing, clapping, or echoing another person's speech). They may overeat compulsively; lose inhibitions, causing them to say or do inappropriate things (sometimes sexual in nature); or become apathetic and experience excessive sleepiness. While they may be cognitively impaired, their memory may stay relatively intact.

Pick's disease, a tauopathy subtype of FTD characterized by hallmark Pick bodies—masses comprised of tau protein that accumulate inside nerve cells, causing them to appear enlarged or balloon-like. Some of the symptoms of this rare neurodegenerative disorder are similar to those of AD, including loss of speech, inappropriate behavior, and trouble with thinking. However, while inappropriate behavior characterizes the early stages of Pick's disease, memory loss is often the first symptom of AD. Antidepressants and antipsychotics can control some of the behavioral symptoms of Pick's disease, but no treatment is available to stop the disease from progressing.

Primary progressive aphasia (PPA)/semantic dementia causes a person to have trouble with expressive and receptive speaking—finding and/or expressing thoughts and/or words. Sometimes a person with PPA cannot name common objects. Problems with memory, reasoning, and judgment are not apparent at first but can develop and progress over time. PPA is a language disorder not to be confused with the aphasia that can result from a stroke. Many people with PPA, though not all, develop symptoms of dementia. In

one form of PPA, called semantic PPA or semantic dementia, a person slowly loses the ability to understand single words and sometimes to recognize the faces of familiar people and common objects.

Progressive supranuclear palsy (PSP) is a rare brain disorder that damages the upper brain stem, including the substantia nigra (a movement control center in the midbrain). This region also is affected in Parkinson's disease, which may explain an overlap in motor symptoms shared by these disorders. Eye movements are especially affected, causing slow and then limited mobility of the eye. The most common early signs and symptoms include loss of balance, unexplained falls, general body stiffness, apathy, and depression. A person with this type of dementia may suddenly laugh or cry very easily (known as pseudobulbar affect). As the disorder progresses, people develop blurred vision and a characteristic vacant stare that involves loss of facial expression. Speech usually becomes slurred, and swallowing solid foods or liquids becomes difficult. PSP gets progressively worse, but people can live a decade or more after the onset of symptoms.

Dextromethorphan, a common ingredient in cough medicine, has been approved for the treatment of pseudobulbar affect.

Frontotemporal dementia with parkinsonism linked to chromosome 17 (FTDP-17), a rare form of dementia that is believed to be inherited from one parent and is linked to a defect in the gene that makes the tau protein. The three core features are behavioral and personality changes, cognitive impairment, and motor symptoms. People with this type of FTD often have delusions, hallucinations, and slowness of movement and tremor as seen in Parkinson's disease. Typical behavioral/personality characteristics include apathy, defective judgment, and compulsive and abusive behavior. Diagnosis of the disorder requires the confirmed presence of clinical features and genetic analysis. Palliative and symptomatic treatments such as physical therapy are the mainstays of management.

Frontotemporal dementia with amyotrophic lateral sclerosis (FTD-ALS) is a combination of bvFTD and ALS, commonly called Lou Gehrig's disease. Symptoms include the behavioral and/or language changes seen in bvFTD as well as the progressive muscle weakness seen in ALS. Symptoms of either disease may appear first, with other symptoms developing over time. Mutations in certain genes have been found in some patients with FTD-ALS.

HUNTINGTON'S DISEASE

This hereditary disorder is caused by a faulty gene for a protein called huntingtin. Symptoms begin around age 30 or 40 years and include abnormal and uncontrollable movements called chorea, as well as gait changes and lack of coordination. Huntington's disease may affect a person's judgment, memory, and other cognitive functions. As the disease progresses, these cognitive problems worsen, and motor difficulties lead to complete loss of ability for self-care. Children of people with Huntington's disease have a 50 percent chance of having the disorder.

LEWY BODY DEMENTIA (DLB)

DLB is one of the more common forms of progressive dementia. Symptoms such as difficulty sleeping, loss of smell, and visual hallucinations often precede movement and other problems by as long as 10 years, which consequently results in DLB going unrecognized or misdiagnosed as a psychiatric disorder until its later stages. Neurons in the substantia nigra that produce dopamine die or become impaired, and the brain's outer layer (cortex) degenerates. Many neurons that remain contain Lewy bodies.

Later in the course of DLB, some signs and symptoms are similar to AD and may include memory loss, poor judgment, and confusion. Other signs and symptoms of DLB are similar to those of Parkinson's disease, including difficulty with movement and posture, a shuffling walk, and changes in alertness and attention. Given these similarities, DLB can be very difficult to diagnose. There is no cure for DLB, but there are drugs that control some symptoms. The medications used to control DLB symptoms can make motor function worse or exacerbate hallucinations.

Parkinson's disease dementia (PDD) is a clinical diagnosis related to DLB that can occur in people with Parkinson's disease. PDD may affect memory, social judgment, language, or reasoning. Autopsy studies show that people with PDD often have amyloid plaques and tau tangles similar to those found in people with AD, though it is not understood what these similarities mean. A majority of people with Parkinson's disease develop dementia, but the time from the onset of movement symptoms to the onset of dementia symptoms varies greatly from person to person. Risk factors for developing PDD include the onset of Parkinson's-related movement symptoms followed by mild cognitive impairment and REM sleep behavior disorder, which involves having frequent vivid nightmares and visual hallucinations.

MIXED DEMENTIA

Autopsy studies looking at the brains of people who had dementia suggest that a majority of those age 80 and older probably had “mixed dementia,” caused by both AD-related neurodegenerative processes and vascular disease-related processes. In fact, some studies indicate that mixed vascular-degenerative dementia is the most common cause of dementia in the elderly. In a person with mixed dementia, it may not be clear exactly how many of a person’s symptoms are due to AD or another type of dementia.

In one study, approximately 40 percent of people who were thought to have AD were found after autopsy to also have some form of cerebrovascular disease. Several studies have found that many of the major risk factors for vascular disease also may be risk factors for AD. Researchers are still working to understand how underlying disease processes in mixed dementia influence each other. It is not clear, for example, if symptoms are likely to be worse when a person has brain changes reflecting multiple types of dementia. Nor do we know if a person with multiple dementias can benefit from treating one type, for example, when a person with AD controls high blood pressure and other vascular disease risk factors.

SECONDARY DEMENTIA/chronic traumatic encephalopathy

Initially known as dementia pugilistica, it is caused by repeated traumatic brain injury (TBI), such as in boxers or in people who suffered multiple concussions while playing a contact sport. People with this condition often develop poor coordination, slurred speech, and other symptoms similar to those seen in Parkinson’s disease, along with dementia, 20 years or more after the TBI events. This form of dementia also is characterized by brain atrophy and widespread deposits of tau aggregates. In some individuals, even just 5 to 10 years beyond the TBI events, behavioral and mood changes may occur. Dementia may not yet be present and the brain may not have atrophied, but small focal deposits of tau are seen in the brain at autopsy.

VASCULAR DEMENTIA

Vascular dementia and vascular cognitive impairment (VCI) are caused by injuries to the vessels supplying blood to the brain. These disorders can be caused by brain damage from multiple strokes or any injury to the small vessels carrying blood to the brain. Dementia risk can be significant even when individuals have suffered only small strokes. Vascular dementia and VCI arise as a result of risk factors that similarly increase the risk for

cerebrovascular disease (stroke), including atrial fibrillation, hypertension, diabetes, and high cholesterol. Vascular dementia also has been associated with a condition called amyloid angiopathy, in which amyloid plaques accumulate in the blood-vessel walls, causing them to break down and rupture. Symptoms of vascular dementia and VCI can begin suddenly and progress or subside during one's lifetime.

Cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL) This inherited form of cardiovascular disease results in a thickening of the walls of small-and medium-sized blood vessels, eventually stemming the flow of blood to the brain. It is associated with mutations of a specific gene called Notch3, which gives instructions to a protein on the surface of the smooth muscle cells that surround blood vessels. CADASIL is associated with multi-infarct dementia, stroke, migraine with aura (migraine preceded by visual symptoms), and mood disorders. The first symptoms can appear in people between ages 20 and 40. Many people with CADASIL are undiagnosed.

People with first-degree relatives who have CADASIL can be tested for genetic mutations to the Notch3 gene to determine their own risk of developing CADASIL. Multi-infarct dementia. This type of dementia occurs when a person has had many small strokes that damage brain cells. One side of the body may be disproportionately affected, and multi-infarct dementia may impair language or other functions, depending on the region of the brain that is affected. Doctors call these “local” or “focal” symptoms, as opposed to the “global” symptoms seen in AD that tend to affect several functions and both sides of the body. When the strokes occur on both sides of the brain, however, dementia is more likely than when stroke occurs on one side of the brain. In some cases, a single stroke can damage the brain enough to cause dementia. This so-called single-infarct dementia is

more common when stroke affects the left side of the brain—where speech centers are located—and/or when it involves the hippocampus, the part of the brain that is vital for memory.

Subcortical vascular dementia, also called Binswanger's disease. This is a rare form of dementia that involves extensive microscopic damage to the small blood vessels and nerve fibers that make up white matter, the “network” part of the brain believed to be critical for relaying messages between regions.

The symptoms of Binswanger's are related to the disruption of subcortical neural circuits involving short-term memory, organization, mood, attention, decision making, and appropriate behavior. A characteristic feature of this disease is psychomotor slowness, such as an increase in the time it takes for a person to think of a letter and then write it on a piece of paper.

Other symptoms include urinary incontinence that is unrelated to a urinary tract condition, trouble walking, clumsiness, slowness, lack of facial expression, and speech difficulties. Symptoms tend to begin after age 60, and they progress in a stepwise manner. People with subcortical vascular disease often have high blood pressure, a history of stroke, or evidence of disease of the large blood vessels in the neck or heart valves. Treatment is aimed at preventing additional strokes and may include drugs to control blood pressure.

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