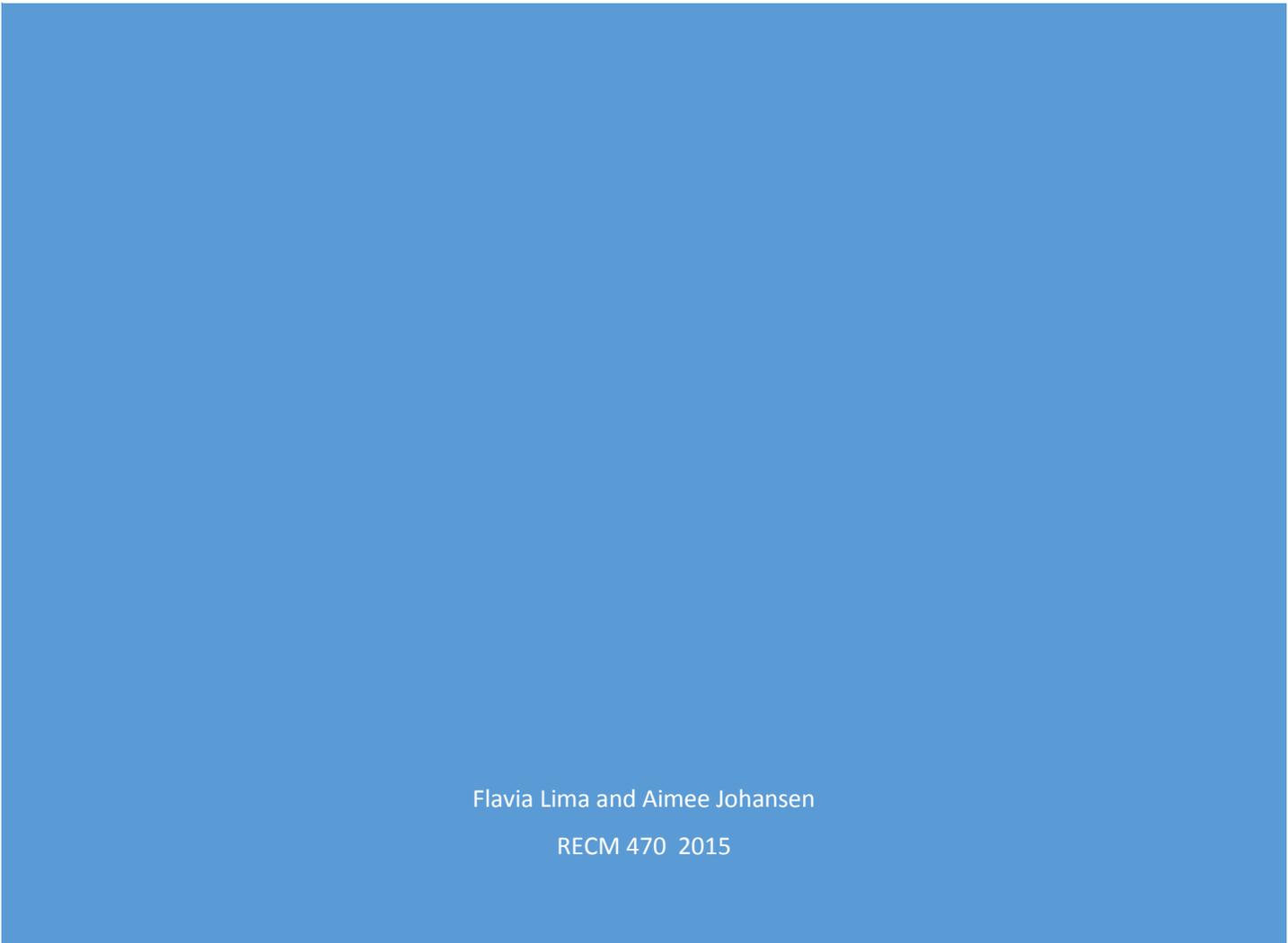




# DISABILITIES ASSOCIATED WITH AGING

Flavia Lima and Aimee Johansen

RECM 470 2015



## Table of Contents

<b>Definition</b> .....	<b>2</b>
Background and Information .....	2
<b>General Practices</b> .....	<b>7</b>
Assessment .....	7
Management .....	7
Prevention .....	9
<b>Alzheimer’s Disease</b> .....	<b>11</b>
Definition .....	11
Signs & Symptoms.....	12
Causes.....	13
Diagnosing .....	15
Treatment .....	15
Research .....	17
Resources .....	17
<b>Parkinson’s Disease</b> .....	<b>19</b>
Definition .....	19
Diagnosing .....	20
Symptoms/Causes/Progression .....	21
Medications and Treatments .....	24
<b>Dementia</b> .....	<b>26</b>
Definition .....	26
Types of Dementia .....	27
Causes.....	34
Diagnosing .....	36
Treatment .....	37
<b>Therapeutic Recreation</b> .....	<b>41</b>
<b>Resources</b> .....	<b>42</b>
Glossary.....	43
<b>References</b> .....	<b>44</b>

# DEFINITION

## World Health Organization<sup>1</sup>

"Disability is an umbrella term, covering impairments, activity limitations, and participation restrictions. An impairment is a problem in body function or structure; an activity limitation is a difficulty encountered by an individual in executing a task or action; while a participation restriction is a problem experienced by an individual in involvement in life situations. Thus disability is a complex phenomenon, reflecting an interaction between features of a person's body and features of the society in which he or she lives."

## Patient<sup>2</sup>

Activities of daily living (ADLs) include personal-care activities such as eating, bathing, dressing, and using the toilet.

Instrumental activities of daily living (IADLs) include household chores, shopping, managing medication, climbing stairs, public transport, finances, and walking. They can be affected by cognitive impairment.

## Background & Information

### Yesterday<sup>3</sup>

- Thirty years ago, America was steadily aging. In 1980, approximately 26.1 million people were 65 years of age or older, compared with 3 million in 1900. And Americans were living notably longer than they had in the past – average life expectancy for a child born in 1980 was 73.7 years, up from 47.3 years in 1900. Disability was on the rise among older people. Studies from the 1970s and early 1980s pointed to modest increases in the prevalence of disability. For example, in 1976, 4.8 million older people reported limitations in the number or kinds of major activities they could undertake.
- It was widely believed that aging invariably brought with it frailty and loss of independence. One study, for example, predicted that technology would save people's lives, but still leave them disabled and an increasing burden on society. However, groundbreaking research from projects such as the Baltimore Longitudinal Study of Aging (<http://www.grc.nia.nih.gov/branches/blsa/blsanew.htm>), initiated in 1958, began to suggest that disease and disability were not inevitable consequences of aging.
- The growth in the aging population, the increase in life expectancy, and concerns about disability led to the founding in 1974 of the National Institute on Aging (NIA) within the National Institutes of Health (NIH). The Institute was charged with “the conduct and support of biomedical, social, and behavioral research, training, health information dissemination, and other programs with respect to the aging process and diseases and other special problems and needs of the aged.”

## Today

- People continue to live longer and the U.S. population is increasingly older. The leading edge of the Baby Boom turns 65 in 2011, part of a rapid growth in population aging in the United States – and worldwide. 39 million people in the United States are age 65 or older, and life expectancy at birth has reached 78.3 years. Most notable is the growth in the population of individuals age 85 and older who are at highest risk for disease and disability.
- Research demonstrates that disease and disability are not an inevitable part of aging. Disability rates can be reduced, as evidenced by data from the National Long Term Care Survey (<http://www.nlctcs.aas.duke.edu/>), which found that between 1982 and 1999, the prevalence of physical disability in older Americans decreased from 26 percent to 20 percent. Additionally, there is evidence from the Health and Retirement Study (<http://hrsonline.isr.umich.edu/>) that the probability of being cognitively impaired at a given age has been decreasing (from the mid-1990s up until at least 2004), although the rapidly increasing population of older adults means that the absolute number of cognitive impaired individuals is still increasing.
- However, it remains unclear whether the decline in disability rates continued since 1999, and researchers are analyzing multiple data sources to ascertain the trend. There is some evidence suggesting that while the decline in disability may have continued among the oldest old (those age 85+), the decline in disability ended or was reversed in the new cohorts recently entering old age.
- Factors thought to have contributed to this decline in disability rates include improved medical treatment (particularly treatments such as beta blockers and ACE inhibitors for cardiovascular disease), positive behavioral changes, more widespread use of assistive technologies, rising education levels, and improvements in socioeconomic status. The NIH supports research to understand the underlying causes of this decline in order to develop behavioral and multi-level interventions to maintain and accelerate this trend.
- Scientists are identifying factors that contribute to healthier aging and longer life expectancy. Epidemiologic studies suggest that lifespan and health are determined by both genetic and environmental influences, with genetics accounting for about 35 percent of lifespan and modifiable environmental factors contributing most to this complex interaction.
- Interventions are being developed to improve how older people function. Researchers at the NIH-supported Claude D. Pepper Older Americans Independence Centers (<https://www.peppercenter.org/public/home.cfm>), for example, have developed effective ways to prevent falls, improve muscle function (size, strength and power), and reduce delirium related to hospital stays. One NIH study dramatically demonstrated that even 90-year-olds can improve muscle strength and mobility with simple weight training exercises.
- However, downward trends in disability may be threatened by recent increases in obesity levels. According to the National Health Interview Survey (<http://www.cdc.gov/nchs/nhis.htm>), the disability rate among people ages 18 to 59 rose significantly from the 1980s through the 1990s, with the growing prevalence of obesity factoring into the trend. Obesity and overweight put people at increased risk for

potentially disabling chronic diseases such as heart disease, type 2 diabetes, high blood pressure, stroke, osteoarthritis, respiratory problems, and some forms of cancer.

## Tomorrow

- Researchers may find ways to identify those most at risk for specific types of disability. NIH investigators have identified several markers, including grip strength, gait (walking) speed, circulating levels of the protein IL-6, and measures of lung function, that can be used to predict the onset of limitations in mobility. Researchers are currently conducting a genome-wide association study to identify genes and genomic regions associated with trajectories of change in each of these markers.
- The National Health and Aging Trends Study (<http://web.jhu.edu/popaging/nhats.html>), a new nationwide NIH-funded study of 12,000 people age 65 and older, will provide data to disentangle the physical, social, technological and environmental factors in disability prevalence, onset, and recovery. The study will also help us understand the social and economic consequences of late-life disability for individuals, families and society.
- The Health and Retirement Study (<http://hrsonline.isr.umich.edu/>), a nationwide NIH-funded survey of more than 22,000 people age 50 and older, is allowing researchers to examine the interactions among physical and mental health, insurance coverage, financial well-being, family support, work status, retirement planning and the impact of these variables on disability. Improved ability to forecast disability trends will help give policymakers more accurate projections of national expenditures for the Social Security and Medicare programs. Researchers will also assess disability risks in understudied populations within the United States, minorities, and the medically underserved.
- Research may bring new treatments to prevent or minimize disability from stroke, diabetes, and other acute and chronic health problems. For example, NIH-supported researchers are developing interventions to improve quadriceps muscle function after total knee replacement and muscle conditioning (muscle size, strength and power) in community dwelling individuals at high risk for falls and mobility disability. Other studies are evaluating the ability of an exercise and health promotion intervention to facilitate maintenance of physical and cognitive function in older adults with mild cognitive impairment (often a precursor condition to Alzheimer's disease). In addition, researchers are conducting a clinical trial of testosterone in men with impaired physical functioning.
- Interventions are being developed to prevent disability in older people. For example, the ongoing Lifestyle Interventions and Independence for Elders (LIFE) Study (<https://www.thelifestudy.org/public/index.cfm>) will assess the effect of an exercise intervention to prevent mobility disability in older adults. NIA also funds a randomized trial of a social engagement intervention, the Experience Corps (<http://www.experiencecorps.org/index.cfm>), which places older volunteers, mostly inner-city residents, in elementary schools in cognitively demanding and socially

productive roles. Preliminary data have shown improvements in both mental and physical health for seniors, as well as benefits for the schools.

## **Epidemiology**

The number of people aged 65 and over is estimated to increase by 65% in the next 25 years, with a doubling of the number of people aged >85 years. Managing older people's health effectively will be important.

The evidence for people aged <85 years tends to suggest that disability in the elderly is reducing, despite an increase in chronic diseases and conditions. For people aged >85 years, the trends regarding disability are less clear.

## **Aetiology**

According to Canadian research, five types of chronic illness contribute largely to disability in people aged over 65 years:

- Foot problems
- Arthritis
- Cognitive impairment
- Heart problems
- Vision

Other common or important problems are:

- Hearing impairment.
- Chronic obstructive pulmonary disease (COPD) - probably more common in the elderly than is recognized.
- Falls and hip fracture.

In frail elderly people, a marked decline in physical and mental function can result from apparently small insults. This has been called the "domino" effect, with a small initial insult leading to a cascade of adverse events.

## **Risk factors**

Frailty in the elderly may be due to a combination of predisposing factors (early childhood development and lifestyle), followed by contributing factors such as physical inactivity, chronic disease, and anorexia/malnutrition in later adulthood.

One review found that the main risk factors for functional disability in elderly people in the community were: lack of schooling, rented housing, chronic diseases, arthritis, diabetes, visual impairment, obesity, poor self-perceived health, cognitive impairment, depression, slow gait, sedentary lifestyle, tiredness while performing daily activities, and limited diversity in social relations.

## **The normal ageing process**

Age is associated with a 1-2% decline in functional ability per year. Sedentary behavior accelerates the loss of performance. Age-associated physiological changes include:

- Changes in body composition - reduction in muscle bulk and lean body mass, known as *sarcopenia*. Body fat may increase.
- Reduction in bone mass and strength with increased risk of fracture; osteoarthritic changes in joints.
- Reduction in blood volume, reduced tolerance of tachycardia; reduced ability to control blood pressure with postural change.
- Reduction in ventilatory capacity.
- Reduction in kidney function; impaired thirst mechanisms which increase susceptibility to dehydration.
- Reduced sensitivity to vitamin D and subsequent reduction in calcium absorption.
- Reduced motility of the large bowel; reduced hepatic mass and blood flow (which may affect hepatic metabolism of drugs).
- Nervous system changes, including reduction in cortical function and reduced motor and sensory peripheral nerve function; changes in autonomic function, including control of heart rate and temperature regulation (failure of normal response mechanisms to hot and cold).
- Reduced elasticity of the eye's lens; high tone hearing impairment.

## Comorbidities

People aged 70 years and over often have one or more chronic conditions. Comorbidities may contribute to disability - for example:

- Stroke can lead to weakness, co-ordination problems, locomotor difficulties and problems of communication and continence.
- Coronary heart disease may lead to heart failure, angina or myocardial infarction.
- Diabetes - complications that can contribute to disability in a variety of ways, eg the contribution of diabetic neuropathy to poor mobility may be underestimated.[13]
- Alzheimer's disease is the most common neurodegenerative disease. By the age of 85 years, 30% of the population has Alzheimer's disease.[14]
- Urinary problems can be disabling, particularly if causing incontinence.
- Depression is often the result of disability but it also makes disability worse. 10-15% of people aged over 65 years living at home are depressed.
- Visual loss is associated with an increased risk of falling.
- Hearing and visual impairment increase the risk of social isolation and resulting depression.
- Falls are associated with injury, pain and loss of function. The prevalence of osteoporosis in the elderly population means that falls are more likely to result in fractures.

# GENERAL PRACTICES

## Assessment<sup>4</sup>

Assessment of a frail or disabled elderly person requires evaluation of:

- The damaged system.
- Other body systems.
- Medication - including polypharmacy.
- Communication.
- Cognition/mood.
- Function (such as ability to perform daily living activities):
  - Activities of daily living (ADLs) - eating/dressing/toileting/mobility.
  - Instrumental activities of daily living (IADLs) - dealing with medication/finances/housework/transportation.
- Environment - both the immediate environment (clothes and housing) and the locality (shops and social facilities).
- Formal and informal supports.
- Social and economic welfare.

Assessment by a specialist geriatrician and/or a multidisciplinary team specializing in elderly care can be useful.

A marked decline in function can be due to relatively small physiological insults, which may result in a frail older person being wrongly labelled as "unable to cope". Bear in mind that early comprehensive geriatric assessment and appropriate treatment may enable such patients to regain lost function.

## Management

### General points

Important aspects of management are:

- Treatment of unstable medical conditions and any treatable problems contributing to the disability.
- Reviewing drug treatment (including polypharmacy).
- Early mobilisation.
- Nutritional support.
- Comprehensive rehabilitation.

Who should be involved in management?

- A multidisciplinary approach can be helpful. This has been shown to be beneficial, eg following stroke and fractured neck of femur. Geriatric day hospitals have been shown to be beneficial in providing care to elderly people with functional decline, although a Cochrane review found they may not have any clear advantage over other forms of comprehensive elderly medical services.

- "Hospital at home" schemes have also been devised, although a Cochrane review found little evidence that they improved functional ability.
- "Case management" by community matrons is a recent development in the care of elderly patients and those with long-term conditions. A recent review of this strategy concluded that this provision is at an early stage of development, and needs to develop effective links with a range of local services. The financial viability of this service is not clear.

## **Aspects of management**

### ***Treat contributing causes***

Do not assume that age-related disability is untreatable. Look for and treat contributing problems (where feasible), such as:

- Uncontrolled cardiac, respiratory or metabolic disease, eg heart failure, hypothyroidism.
- Reversible causes of hearing loss, eg wax.
- Potentially treatable neurological disease, eg tumors.

### ***Drug treatment***

- Medication can contribute to both the problem of disability and the solution.
- Polypharmacy and increased susceptibility to drug side-effects are some of the issues surrounding medication in older people. See the separate Prescribing for the Older Patient article that discusses this topic in detail.
- Vitamin D deficiency should be recognized and treated in the elderly. The Department of Health has recommended that people over the age of 65 years take vitamin D supplements.

### ***Surgical treatment***

- Age alone is not a contra-indication for surgery.
- Operations such as joint replacement, cataract surgery and surgery for prostatic hypertrophy are frequently performed on the elderly to reduce disability.

### ***Provision of aids and appliances***

- Occupational therapy and the provision of aids can improve the quality of life. Home adjustments such as grip rails, stair lifts and removal of dangers such as loose carpets or inappropriate footwear can be helpful.
- Aids should be used to make the most of impaired vision or hearing.
- Glasses, low vision aids such as magnifying glasses, large-print materials, talking clocks and watches, telephones with large numbers, audio books, safety measures, such as raised-dot dials on kitchen equipment, may all be helpful.
- Hearing aids can greatly improve quality of life.
- Adapted safety devices may be needed (eg flashing light on telephone or smoke alarm).

### ***Pain management***

A paper discussing chronic pain in elderly people suggests that persistent pain in elderly patients is not simply a chronologically older version of younger pain. They suggest that interventions such as a 'mindfulness-based stress reduction program can be helpful.

Appropriate exercise can be part of pain management in some conditions, eg osteoarthritis.

### ***Social and environmental interventions***

These may reduce the impact of the disability - for example:

- Financial support - eg access to benefits and grants.
- Social support - eg day centers, social activities and befriending.
- Housing support - appropriate accommodation can support independence and increase functional ability.

## **Prevention**

The National Service Framework states that there is strong evidence of benefit to older people from:

- Increasing physical activity.
- Improved diet and nutrition.
- Immunization and management programs for influenza.

### **Exercise**

Adapted exercise is beneficial for strength, mobility and balance, and may reduce the risk of falls. This applies even to frail older people. Indirectly, physical activity may also increase wellbeing, social activity and mental health.

### ***Evidence on the role of exercise in preventing disability***

In terms of preventing disability, some trials involving physical exercise interventions reported positive outcomes for disability. However, differences between the trials can make it difficult to review the evidence or to make precise recommendations.

A review disability from hip fracture suggested physical activity can protect against the risk of hip fracture among community-dwelling older adults. This may be via increased levels of vitamin D, or through the improvement of bone quality.

One editorial proposes 'assertive screening', using a single question to identify middle-aged and elderly people who are sedentary. These people could be invited to participate in lifestyle interventions including a prescription for exercise. It is suggested that a single question about a fall in the previous year is a method of identifying those who will benefit most.

### ***How much exercise?***

- The goal is to work towards 30 minutes of at least moderate-intensity physical activity on at least five days of the week.

- Two 15-minute periods of moderate activity daily may be a good way to start. If that is too much, take a 'little and often' approach, advising a gradual increase starting with just three minutes.
- The ideal is a combination of endurance exercises, strength exercises and stretching/balance/co-ordination exercises.
- It is never too late to start, and any activity is better than none.
- Adequate warm-up is important, and safe exercises/movement patterns should be chosen

## **Nutrition**

- Elderly people have relatively more body fat and less lean body mass, resulting in lower metabolic rates. Therefore, calorie needs are reduced, so the diet needs proportionately more protein, essential fats and micronutrients. Improving nutritional status (adequate calories and protein) can help to reduce sarcopenia and frailty in the elderly.
- Avoiding obesity is also beneficial.
- Aim to meet minimum nutritional requirements, provide adequate dietary fibre, and address specific disease risks such as cardiovascular disease, stroke, diabetes and osteoporosis.
- Vitamin D may help prevent muscle weakness, falls and fractures, but adequate doses must be used.
- Oral health and provision of dental treatment are important.
- Hospital nutrition - Age UK has campaigned for greater awareness of the problem of malnutrition in hospitalized elderly patients. Practical steps have been suggested, eg a 'red tray' system to indicate which patients need assistance at mealtimes.
- Folic acid ± vitamin B12 has been suggested as possibly benefiting cognitive function in elderly people. However, a Cochrane review concluded that there is no consistent evidence either way, and more research is needed.

## **Screening and case finding**

Are health checks useful?

The value of health checks for older people is uncertain:

- Annual checks by a nurse visit have shown benefit in mortality, but not in UK studies.
- Case finding targets proactive care on individuals with a high level of need. Although interventions in this group are appreciated, a reduction in mortality or hospital admissions has not been shown.
- Screening programs probably need to be intensive and sustained, if they are to deliver benefits.
- There is conflicting evidence regarding the benefits of preventive home visits to the elderly.
- One Canadian study looked at intervention by the emergency department, which identified high-risk elderly patients and referred them for community care. Better clinical outcomes were observed.

The British Geriatrics Society suggests that:

- A thorough assessment is needed for elderly people experiencing disability or a crisis.
- Otherwise, elderly people should be encouraged to follow healthy ageing advice.

## *NHS screening and prevention services for the elderly*

The Department of Health recommends the following screening for elderly people:

- Annual influenza immunization (and pneumococcal vaccine for those with chronic conditions such as COPD).
- Regular eye checks - free for people aged over 60; 2-yearly to age 60, annually from age 70.
- Hearing test - if a person's hearing is problematic or deteriorating.
- Bowel cancer screening - testing kits are sent every two years to people aged 60-69 who are registered with a GP. People aged >69 can request a kit every two years.
- Abdominal aortic aneurysm screening - is being made available to all men aged 65.
- Mammogram 3-yearly (over age 70 this must be requested by the woman).
- Cervical screening - women over age 65 are screened only if previous screening was abnormal or not done.

Healthy diet and lifestyle, including smoking cessation, should also be promoted.

## ALZHEIMER'S DISEASE<sup>5</sup>



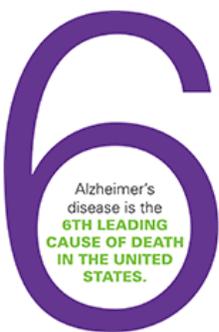
It's the only cause of death in the top 10 in America that **CANNOT BE PREVENTED, CURED OR SLOWED.**



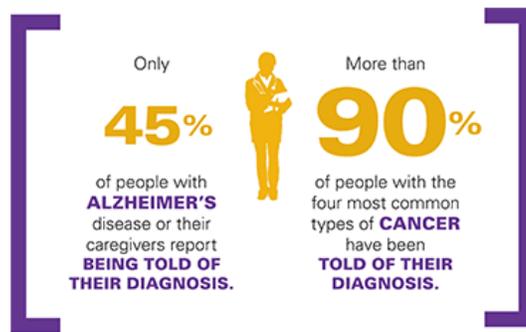
**ALMOST TWO THIRDS** of Americans with Alzheimer's disease are women.



**1 IN 3 SENIORS** dies with Alzheimer's or another dementia.



Alzheimer's disease is the **6TH LEADING CAUSE OF DEATH IN THE UNITED STATES.**



By 2050, these costs could rise as high as **\$1.1 TRILLION.**



In 2015, Alzheimer's and other dementias will cost the nation **\$226 BILLION.**

## Definition

Alzheimer's disease is an irreversible, progressive brain disease that slowly destroys memory and thinking skills, and eventually even the ability to carry out the simplest tasks. In most people

with Alzheimer's, symptoms first appear after age 65. Estimates vary, but experts suggest that as many as 5 million Americans age 65 and older may have Alzheimer's disease.

Alzheimer's disease is the most common cause of dementia among older people. 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. Dementia ranges in severity from the mildest stage, when it is just beginning to affect a person's functioning, to the most severe stage, when the person must depend completely on others for basic activities of daily living.

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 tangles). Plaques and tangles in the brain are two of the main features of Alzheimer's disease. The third is the loss of connections between nerve cells (neurons) in the brain.

### Changes in the Brain in Alzheimer's Disease



*As Alzheimer's disease progresses, neurofibrillary tangles (shown in blue) and amyloid plaques spread throughout the brain.*

Although we still don't know how the Alzheimer's disease process begins, it seems likely that damage to the brain starts a decade or more before problems become evident. During the preclinical stage of Alzheimer's disease, people are free of symptoms but toxic changes are taking place in the brain. Abnormal deposits of proteins form amyloid plaques and tau tangles throughout the brain, and once-healthy neurons begin to work less efficiently. Over time, neurons lose their ability to function and communicate with each other, and eventually they die.

Before long, the damage spreads to a nearby structure in the brain called the hippocampus, which is essential in forming memories. As more neurons die, affected brain regions begin to shrink. By the final stage of Alzheimer's, damage is widespread, and brain tissue has shrunk significantly.

### Very Early Signs and Symptoms

Memory problems are typically one of the first warning signs of cognitive loss, possibly due to the development of Alzheimer's disease. Some people with memory problems have a condition called amnesic mild cognitive impairment (MCI). People with this condition have more memory problems than normal for people their age, but their symptoms are not as severe as those seen in people with Alzheimer's disease. Other recent studies have found links between some movement difficulties and MCI. Researchers also have seen links between MCI and some problems with the sense of smell. The ability of people with MCI to perform normal daily activities is not

significantly impaired. However, more older people with MCI, compared with those without MCI, go on to develop Alzheimer's.

A decline in other aspects of cognition, such as word-finding, vision/spatial issues, and impaired reasoning or judgment, may also signal the very early stages of Alzheimer's disease. Scientists are looking to see whether brain imaging and biomarker studies, for example, of people with MCI and those with a family history of Alzheimer's, can detect early changes in the brain like those seen in Alzheimer's. Initial studies indicate that early detection using biomarkers and imaging may be possible, but findings will need to be confirmed by other studies before these techniques can be used to help with diagnosis in everyday medical practice.

These and other studies offer hope that someday we may have tools that could help detect Alzheimer's early, track the course of the disease, and monitor response to treatments.

### **Mild Alzheimer's Disease**

As Alzheimer's disease progresses, memory loss worsens, and changes in other cognitive abilities are evident. Problems can include, for example, getting lost, trouble handling money and paying bills, repeating questions, taking longer to complete normal daily tasks, using poor judgment, and having some mood and personality changes. People often are diagnosed in this stage.

### **Moderate Alzheimer's Disease**

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 tasks that involve multiple steps (such as getting dressed), or cope with new situations. They may have hallucinations, delusions, and paranoia, and may behave impulsively.

### **Severe Alzheimer's Disease**

By the final stage, plaques and tangles have spread throughout the brain, and brain tissue has shrunk 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.

## **Causes**

Scientists don't yet fully understand what causes Alzheimer's disease, but it has become increasingly clear that it develops because of a complex series of events that take place in the brain over a long period of time. It is likely that the causes include some mix of genetic, environmental, and lifestyle factors. Because people differ in their genetic make-up and lifestyle, the importance of any one of these factors in increasing or decreasing the risk of developing Alzheimer's may differ from person to person.

## **The Basics of Alzheimer's**

Scientists are conducting studies to learn more about plaques, tangles, and other features of Alzheimer's disease. Advances in brain imaging techniques now allow researchers to visualize abnormal levels of beta-amyloid and tau proteins in the living brain. Scientists are also exploring the very earliest steps in the disease process. Findings from these studies will help them understand the causes of Alzheimer's.

One of the great mysteries of Alzheimer's disease is why it largely strikes older adults. Research on how the brain changes normally with age 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, the production of unstable molecules called free radicals, and mitochondrial dysfunction (a breakdown of energy production within a cell).

## **Genetics**

Early-onset Alzheimer's is a rare form of the disease. It occurs in people age 30 to 60 and represents less than 5 percent of all people who have Alzheimer's disease. Most cases of early-onset Alzheimer's are familial Alzheimer's disease, caused by changes in one of three known genes inherited from a parent. For more information, see NIA's *Early-Onset Alzheimer's Disease: A Resource List*.

Most people with Alzheimer's disease have "late-onset" Alzheimer's, which usually develops after age 60. Many studies have linked the apolipoprotein E (APOE) gene to late-onset Alzheimer's. This gene has several forms. One of them, APOE  $\epsilon$ 4, seems to increase a person's risk of getting the disease. However, carrying the APOE  $\epsilon$ 4 form of the gene does not necessarily mean that a person will develop Alzheimer's disease, and people carrying no APOE  $\epsilon$ 4 can also develop the disease.

Most experts believe that additional genes may influence the development of late-onset Alzheimer's. Scientists around the world are searching for these genes, and have identified a number of common genes in addition to APOE  $\epsilon$ 4 that may increase a person's risk for late-onset Alzheimer's.

For more about this area of research, see NIA's *Alzheimer's Disease Genetics Fact Sheet*.

## **Environmental/Lifestyle Factors**

Research also suggests that a host of factors beyond basic genetics may play a role in the development and course of Alzheimer's disease. There is a great deal of interest, for example, in associations between cognitive decline and vascular and metabolic conditions such as heart disease, stroke, high blood pressure, diabetes, and obesity. Understanding these relationships and testing them in clinical trials will help us understand whether reducing risk factors for these conditions may help with Alzheimer's as well.

Further, a nutritious diet, physical activity (PDF, 871K), social engagement, and mentally stimulating pursuits can all help people stay healthy as they age. New research suggests the possibility that these and other factors also might help to reduce the risk of cognitive decline and

Alzheimer's disease. Clinical trials of specific interventions are underway to test some of these possibilities.

## Diagnosing

Alzheimer's disease can be definitively diagnosed only after death, by linking clinical measures with an examination of brain tissue and pathology in an autopsy. But doctors now have several methods and tools to help them determine fairly accurately 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 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) or magnetic resonance imaging (MRI), to distinguish Alzheimer's from other possible causes for symptoms, like stroke or tumor

These tests may be repeated to give doctors information about how the person's memory is changing over time.

Early, accurate diagnosis is beneficial for several reasons. It can tell people whether their symptoms are from Alzheimer's or another cause, such as stroke, tumor, Parkinson's disease, sleep disturbances, side effects of medications, or other conditions that may be treatable and possibly reversible.

Beginning treatment early on in the disease process can help preserve function for some time, even though the underlying disease process cannot be changed. Having an early diagnosis also helps families plan for the future, make living arrangements, take care of financial and legal matters, and develop support networks.

In addition, an early diagnosis can provide greater opportunities for people to get involved in clinical trials. In a typical clinical trial, scientists test a drug or treatment to see if that intervention is effective and for whom it would work best.

## Treatment

Alzheimer's disease is complex, and it is unlikely that any one intervention will be found to delay, prevent, or cure it. That's why current approaches in treatment and research focus on several different aspects, including helping people maintain mental function, managing behavioral symptoms, and slowing or delaying the symptoms of disease.

### **Maintaining Mental Function**

Four medications are approved by the U.S. Food and Drug Administration to treat 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 chemicals that transmit messages between neurons). They may help maintain thinking, memory, and speaking skills, and help with certain behavioral problems. However, these drugs don't change the underlying disease process, are effective for some but not all people, and may help only for a limited time.

## **Managing Behavioral Symptoms**

Common behavioral symptoms of Alzheimer's include sleeplessness, agitation, wandering, anxiety, anger, and depression. Scientists are learning why these symptoms occur and are studying new treatments—drug and non-drug—to manage them. Treating behavioral symptoms often makes people with Alzheimer's more comfortable and makes their care easier for caregivers.

## **Slowing, Delaying, or Preventing Alzheimer's Disease**

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 looking at many possible interventions, such as immunization therapy, cognitive training, physical activity, antioxidants, and the effects of cardiovascular and diabetes treatments.

### **Supporting 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, changing family roles, and difficult decisions about placement in a care facility can be hard to handle. Researchers have learned much about Alzheimer's caregiving, and studies are helping to develop new ways to support caregivers.

Becoming well-informed about the disease is one important long-term strategy. Programs that teach families about the various stages of Alzheimer's and about flexible and practical strategies for dealing with difficult caregiving situations provide vital help to those who care for people with Alzheimer's.

Developing good coping skills and a strong support network of family and friends also are important ways that caregivers can help themselves handle the stresses of caring for a loved one with Alzheimer's disease. For example, staying physically active provides physical and emotional benefits.

Some Alzheimer's caregivers have found that participating in a support group is a critical lifeline. These support groups allow caregivers to find respite, express concerns, share experiences, get tips, and receive emotional comfort. Many organizations, such as those listed in the "For More Information" section, sponsor in-person and online support groups across the country. There are a growing number of groups for people in the early stage of Alzheimer's and their families. Support networks can be especially valuable when caregivers face the difficult

decision of whether and when to place a loved one in a nursing home or assisted living facility. For more information about at-home caregiving, see [\*Caring for a Person with Alzheimer's Disease: Your Easy-to-Use Guide from the National Institute on Aging\*](#).

## Research

Thirty years ago, we knew very little about Alzheimer's disease. Since then, scientists have made important advances. Research supported by NIA and other organizations has expanded knowledge of brain function in healthy older people, identified ways we might lessen normal age-related declines in mental function, and deepened our understanding of the disease. Many scientists and physicians are now working together to untangle the genetic, biological, and environmental factors that, over many years, ultimately result in Alzheimer's. This effort is bringing us closer to better managing and, ultimately, preventing this devastating disease.

## Resources

### For More Information

To learn about support groups, services, research centers, research studies, and publications about Alzheimer's disease, contact the following resources:

#### **Alzheimer's Disease Education and Referral (ADEAR) Center**

P.O. Box 8250

Silver Spring, MD 20907-8250

1-800-438-4380 (toll-free)

[www.nia.nih.gov/alzheimers](http://www.nia.nih.gov/alzheimers)

The National Institute on Aging's ADEAR Center offers information and [publications](#) for families, caregivers, and professionals on diagnosis, treatment, patient care, caregiver needs, long-term care, education and training, and research related to Alzheimer's disease. Staff members answer telephone, email, and written requests and make referrals to local and national resources. Visit the ADEAR website to learn more about Alzheimer's and other dementias, find clinical trials, and [sign up for email updates](#).

#### **Alzheimer's Association**

225 North Michigan Avenue, Floor 17

Chicago, IL 60601-7633

1-800-272-3900 (toll-free)

1-866-403-3073 (TDD/toll-free)

[www.alz.org](http://www.alz.org)

**Alzheimer's Foundation of America**

322 Eighth Avenue, 7th Floor

New York, NY 10001

1-866-AFA-8484 (1-866-232-8484; toll-free)

[www.alzfdn.org](http://www.alzfdn.org)

**Eldercare Locator**

1-800-677-1116 (toll-free)

[www.eldercare.gov](http://www.eldercare.gov)

**Family Caregiver Alliance**

785 Market Street, Suite 750

San Francisco, CA 94103

1-800-445-8106 (toll-free)

[www.caregiver.org](http://www.caregiver.org)

**NIH Senior Health**

[www.nihseniorhealth.gov/alzheimersdisease/toc.html](http://www.nihseniorhealth.gov/alzheimersdisease/toc.html)

Alzheimer's Disease Education & Referral (ADEAR) Center

A service of the National Institute on Aging

**National Institutes of Health**

*NIH...Turning Discovery Into Health®*

U.S. Department of Health and Human Services

Publication Date: September 2012

Page Last Updated: March 27, 2015

# PARKINSON'S DISEASE<sup>6</sup>

## Definition

Parkinson's disease (PD) is a chronic and progressive movement disorder, meaning that symptoms continue and worsen over time. Nearly one million people in the US are living with Parkinson's disease. The cause is unknown, and although there is presently no cure, there are treatment options such as medication and surgery to manage its symptoms.

Parkinson's involves the malfunction and death of vital nerve cells in the brain, called neurons. Parkinson's primarily affects neurons in the area of the brain called the substantia nigra. Some of these dying neurons produce dopamine, a chemical that sends messages to the part of the brain that controls movement and coordination. As PD progresses, the amount of dopamine produced in the brain decreases, leaving a person unable to control movement normally.

The specific group of symptoms that an individual experiences varies from person to person. Primary motor signs of Parkinson's disease include the following.

- **tremor** of the hands, arms, legs, jaw and face
- **bradykinesia** or slowness of movement
- **rigidity** or stiffness of the limbs and trunk
- **postural instability** or impaired balance and coordination

Scientists are also exploring the idea that loss of cells in other areas of the brain and body contribute to Parkinson's. For example, researchers have discovered that the hallmark sign of Parkinson's disease — clumps of a protein alpha-synuclein, which are also called Lewy Bodies — are found not only in the mid-brain but also in the brain stem and the olfactory bulb.

These areas of the brain correlate to nonmotor functions such as sense of smell and sleep regulation. The presence of Lewy bodies in these areas could explain the nonmotor symptoms experienced by some people with PD before any motor sign of the disease appears. The intestines also have dopamine cells that degenerate in Parkinson's, and this may be important in the gastrointestinal symptoms that are part of the disease.

## To Learn More:

- Browse information about the [symptoms of Parkinson's](#).
- Have you been diagnosed with a Parkinson's Plus Syndrome? Read [Understanding Atypical Parkinsonism](#) – to better understand your [diagnosis](#) and how it may differ from a diagnosis of Parkinson's disease.
- [Order PDF's free publications](#), including the Second Edition of the *Parkinson's Disease Resource List*.

## Diagnosing

Making an accurate diagnosis of Parkinson's — particularly in its early stages — is difficult, but a skilled practitioner can come to a reasoned conclusion that it is PD. You may have experienced this frustration. Perhaps it took years for you to receive a diagnosis. Perhaps you have been diagnosed, but with *Parkinsonism*, not Parkinson's, and are confused about the implications.

### How is Parkinson's Diagnosed?

Often, the diagnosis of Parkinson's is first made by an internist or family physician. Many people seek an additional opinion from a neurologist with experience and specific training in the assessment and treatment of Parkinson's disease — referred to as a movement disorder specialist.

To diagnose Parkinson's, the physician takes a careful neurological history and performs an examination. There are no standard diagnostic tests for Parkinson's, so the diagnosis rests on the clinical information provided by the person with Parkinson's and the findings of the neurological exam.

- The doctor looks to see if your expression is animated.
- Your arms are observed for tremor, which is present either when they are at rest, or extended.
- Is there stiffness in your limbs or neck?
- Can you rise from a chair easily?
- Do you walk normally or with short steps, and do your arms swing symmetrically? The doctor will pull you backwards.
- How quickly are you able to regain your balance?

The main role of any additional testing is to exclude other diseases that imitate Parkinson's disease, such as stroke or hydrocephalus. Very mild cases of PD can be difficult to confirm, even by an experienced neurologist. This is in part because there are many neurological conditions that mimic the appearance of Parkinson's.

A person's good response to levodopa (which temporarily restores dopamine action in the brain) may support the diagnosis. But this is not relevant if your doctor thinks you do not need any medication at this time. If you are in doubt of your diagnosis or if you need further information, you may want to seek a second opinion.

PDF recommends that a person with symptoms resembling those of PD consider making an appointment with a movement disorder specialist. To find a specialist in your community, call PDF's HelpLine at (800) 457-6676 from Monday to Friday, 9 AM EDT to 5 PM EDT and our staff can help you locate one.

### Why Aren't There Tests to Diagnose Parkinson's?

There is no standard diagnostic test for Parkinson's. Researchers are working to develop an accurate "biological marker," such as a blood test or an imaging scan. To date, the best objective

testing for PD consists of specialized brain scanning techniques that can measure the dopamine system and brain metabolism. But these tests are performed only in specialized imaging centers and can be very expensive.

### **To Learn More:**

- Visit the Living with Parkinson's section to learn more about [You and Your Doctor](#)
- Download our fact sheet, [Understanding Atypical Parkinsonism](#)
- Learn general facts about Parkinson's disease by reading, [Parkinson's FAQ](#)

## Symptoms

The diagnosis of PD depends upon the presence of one or more of the four most common motor symptoms of the disease. In addition, there are other secondary and nonmotor symptoms that affect many people and are increasingly recognized by doctors as important to treating Parkinson's.

Each person with Parkinson's will experience symptoms differently. For example, many people experience tremor as their primary symptom, while others may not have tremors, but may have problems with balance. Also, for some people the disease progresses quickly, and in others it does not.

By definition, Parkinson's is a progressive disease. Although some people with Parkinson's only have symptoms on one side of the body for many years, eventually the symptoms begin on the other side. Symptoms on the other side of the body often do not become as severe as symptoms on the initial side.

## Causes

### **What Causes Parkinson's?**

To date, despite decades of intensive study, the causes of Parkinson's remain unknown. Many experts think that the disease is caused by a combination of genetic and environmental factors, which may vary from person to person.

In some people, genetic factors may play a role; in others, illness, an environmental toxin or other event may contribute to PD. Scientists have identified aging as an important risk factor; there is a **two to four percent risk** for Parkinson's among people over age 60, compared with one to two percent in the general population.

The chemical or genetic trigger that starts the cell death process in dopamine neurons is the subject of intense scientific study. Many believe that by understanding the sequence of events that leads to the loss of dopamine cells, scientists will be able to develop treatments to stop or reverse the disease

Read more below about each of these:

- [Genetic Factors](#)

- [Environmental Factors](#)

## **Genetic Factors**

The vast majority of Parkinson's cases are not directly inherited. About 15 to 25 percent of people with Parkinson's report having a relative with the disease. In large population studies, researchers have found that people with an affected first-degree relative, such as a parent or sibling, have a four to nine percent higher chance of developing PD, as compared to the general population. This means that if a person's parent has PD, his or her chances of developing the disease are slightly higher than the risk among the general population.

Researchers have discovered several gene mutations that can cause the disease directly, but these affect only a small number of families. Some of these mutations involve genes that play a role in dopamine cell functions. Parkinson's has developed at an early age in individuals with mutations in genes for parkin, PINK1, LRRK2, DJ-1, and glucocerebrosidase, among others.

Because genetic forms of a disease can be studied in great detail in the laboratory, and because understanding the rare genetic forms of Parkinson's may help us to understand more common forms of the disease, genetics is currently the subject of intense research.

## **Environmental Factors**

Some scientists have suggested that Parkinson's disease may result from exposure to an environmental toxin or injury. Epidemiological research has identified several factors that may be linked to Parkinson's, including rural living, well water, manganese and pesticides.

Some studies have demonstrated that prolonged occupational exposure to certain chemicals is associated with an elevated risk of PD. These include the insecticides permethrin and beta-hexachlorocyclohexane (beta-HCH), the herbicides paraquat and 2,4-dichlorophenoxyacetic acid and the fungicide maneb. In 2009, the US Department of Veterans Affairs added Parkinson's to a list of diseases possibly associated with exposure to Agent Orange.

A synthetic neurotoxin agent called MPTP can also cause immediate and permanent parkinsonism. The compound was discovered in the 1980s in individuals who injected themselves with a synthetic form of heroin contaminated with MPTP. Cases of MPTP-induced Parkinson's in the general population are exceedingly rare.

It is noted that a simple exposure to an environmental toxin is never enough to cause Parkinson's. Most people exposed to a toxin do not develop the disease. In fact, there is no conclusive evidence that any environmental factor, alone, can be considered a cause of the disease.

However, environmental factors have been helpful in studying laboratory models of Parkinson's. Scientists continue to pursue these clues to understand why Parkinson's disease occurs.

## Progression

The progression of Parkinson's disease varies among different individuals. Parkinson's is chronic and slowly progressive, meaning that symptoms continue and worsen over a period of years. Parkinson's is not considered a fatal disease. And the way that it progresses is different for everyone:

- Movement symptoms vary from person to person, and so does the rate at which they progress.
- Some are more bothersome than others depending on what a person normally does during the day.
- Some people with Parkinson's live with mild symptoms for many years, whereas others develop movement difficulties more quickly.
- Nonmotor symptoms also are very individualized, and they affect most people with Parkinson's at all stages of disease. Some people with Parkinson's find that symptoms such as depression or fatigue interfere more with daily life than do problems with movement.

## Rating Scales

That said, there are tools that your doctor may use to understand the progression of your Parkinson's. The stages of Parkinson's correspond both to the severity of movement symptoms and to how much the disease affects a person's daily activities. The most commonly used rating scales are focused on the motor symptoms, but new scales include information on non-motor symptoms (such as problems with sense of smell).

1. The first, known as Hoehn and Yahr, will rate your symptoms on a scale of 1 to 5. On this scale, depending on a person's difficulties, 1 and 2 represent early-stage, 2 and 3 mid-stage, and 4 and 5 advanced-stage Parkinson's.
2. Another scale commonly used to assess the progression of Parkinson's is the United Parkinson's Disease Rating Scale (UPDRS). It is more comprehensive than the Hoehn and Yahr scale, which focuses on movement symptoms. In addition to these, the UPDRS takes into account cognitive difficulties, ability to carry out daily activities, and treatment complications.

## Severity of Parkinson's

Below are some descriptions of mild, moderate and advanced Parkinson's. As disease progresses differently in different people, many do not progress to the advanced stage.

### Mild Parkinson's

- Movement symptoms may be inconvenient, but do not affect daily activities
- Movement symptoms, often tremor, occur on one side of the body

- Friends may notice changes in a person’s posture, walking ability or facial expression
- Parkinson's medications suppress movement symptoms effectively
- Regular exercise improves and maintains mobility, flexibility, range of motion and balance, and also reduces depression and constipation

## **Moderate Parkinson’s**

- Movement symptoms occur on both sides of the body
- The body moves more slowly
- Trouble with balance and coordination may develop
- “Freezing” episodes — when the feet feel stuck to the ground — may occur
- Parkinson's medications may “wear off” between doses
- Parkinson's medications may cause side effects, including dyskinesias (involuntary movements)
- Regular exercise, perhaps with physical therapy, continues to be important for good mobility and balance
- Occupational therapy may provide strategies for maintaining independence

## **Advanced Parkinson’s**

- Great difficulty walking; in wheelchair or bed most of the day
- Not able to live alone
- Assistance needed with all daily activities
- Cognitive problems may be prominent, including hallucinations and delusions
- Balancing the benefits of medications with their side effects becomes more challenging

At all stages of Parkinson's, effective therapies are available to ease symptoms and make it possible for people with Parkinson's to live well.

## **Medications & Treatments**

There are many medications available to treat the symptoms of Parkinson’s, although none yet that actually reverse the effects of the disease.

It is common for people with PD to take a variety of these medications – all at different doses and at different times of day - in order to manage the symptoms of the disease.

While keeping track of medications can be a challenging task, understanding your medications and sticking to a schedule will provide the greatest benefit from the drugs and avoid unpleasant “off” periods due to missed doses.

Read more to understand each type of medication, its dosing and side effects. Interested in learning more about medications in the pipeline?

## **Clinical Trials**

### **What are Clinical Trials?**

A clinical trial is a human research study designed by scientists and medical experts to answer questions about a disease and potential new therapies. They are an essential and necessary component of the scientific research process. Simply put, there is no other way for research to show that a proposed treatment works.

## **Statistics on Parkinson's**

### **Who Has Parkinson's?**

- As many as one million Americans live with Parkinson's disease, which is more than the combined number of people diagnosed with multiple sclerosis, muscular dystrophy and Lou Gehrig's disease.
- Approximately 60,000 Americans are diagnosed with Parkinson's disease each year, and this number does not reflect the thousands of cases that go undetected.
- An estimated seven to 10 million people worldwide are living with Parkinson's disease.
- Incidence of Parkinson's increases with age, but an estimated four percent of people with PD are diagnosed before the age of 50.
- Men are one and a half times more likely to have Parkinson's than women.

### **What Does Parkinson's Cost?**

- The combined direct and indirect cost of Parkinson's, including treatment, social security payments and lost income from inability to work, is estimated to be nearly \$25 billion per year in the United States alone.
- Medication costs for an individual person with PD average \$2,500 a year, and therapeutic surgery can cost up to \$100,000 dollars per patient.

### **What's Next?**

Now that you have learned the basic of Parkinson's, what's next? Browse some of the resources below to ensure you have the most up-to-date information on Parkinson's [anddf.org/about\\_pd](http://anddf.org/about_pd)

# DEMENTIA<sup>7</sup>

## Definition

A diagnosis of dementia can be frightening for those affected by the syndrome, their family members, and caretakers. Learning more about dementia can help. This booklet provides a general overview of various types of dementia, describes how the disorders are diagnosed and treated, and offers highlights of research that is supported by the National Institute of Neurological Disorders and Stroke and the National Institute on Aging, both part of the National Institutes of Health (NIH).

**Alzheimer’s disease (AD)** is the most common form of dementia in those over the age of 65. As many as 5 million Americans age 65 and older may have AD, and that number is expected to double for every 5-year interval beyond age 65. But Alzheimer’s is only one of many dementia disorders; an estimated 20 to 40 percent of people with dementia have some other form of the disorder. Among all people with dementia, many are believed to have a mixed type of dementia that can involve more than one of the disorders.

Age is the primary risk factor for developing dementia. For that reason, the number of people living with dementia could double in the next 40 years with an increase in the number of Americans who are age 65 or older—from 40 million today to more than 88 million in 2050. Regardless of the form of dementia, the personal, economic, and societal demands can be devastating.

Research over the past 30 years has helped us learn more about dementia—possible causes, who is at risk, and how it develops and affects the brain. This work offers the hope of better drugs and treatments for these disorders.

*\*Terms in Italics are defined in the **glossary**.*

## The Basics of Dementia

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 without any signs of dementia.

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 tasks.

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

Various disorders and factors contribute to the development of dementia. Neurodegenerative disorders such as AD, frontotemporal disorders, and Lewy body dementia result in a progressive and irreversible loss of neurons and brain functions. Currently, there are no cures for these progressive neurodegenerative disorders.

However, other types of dementia can be halted or even reversed with treatment. Normal pressure hydrocephalus, for example, often resolves when excess cerebrospinal fluid in the brain is drained via a shunt and rerouted elsewhere in the body. Cerebral vasculitis responds to aggressive treatment with immunosuppressive drugs. In rare cases, treatable infectious disorders can cause dementia. Some drugs, vitamin deficiencies, alcohol abuse, depression, and brain tumors can cause neurological deficits that resemble dementia. Most of these causes respond to treatment.

Some types of dementia disorders are described below.

### **Tauopathies**

In some dementias, a protein called tau clumps together inside nerve cells in the brain, causing the cells to stop functioning properly and die. Disorders that are associated with an accumulation of tau are called tauopathies.

In AD, the tau protein becomes twisted and aggregates to form bundles, called neurofibrillary tangles, inside the neurons. Abnormal clumps (plaques) of another protein, called amyloid, are prominent in spaces between brain cells and are a hallmark of the disease. Both plaques and tangles are thought to contribute to reduced function and nerve-cell death in AD, but scientists do not fully understand this relationship. It is not clear, for example, if the plaques and tangles cause the disorder, or if their presence flags some other process that leads to neuronal death in AD.

Other types of tauopathies include the following disorders:

**Corticobasal degeneration (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.

**Frontotemporal disorders (FTD)** are caused by a family of brain diseases that primarily affect the frontal and temporal lobes of the brain; they account for up to 10 percent of all dementia cases. Some, but not all, forms of FTD are considered tauopathies. In some cases, FTD is associated with mutations in the gene for tau (MAPT), and tau aggregates are present. However, other forms of FTD are associated with aggregates of the protein TDP-43, a mutated protein found among people with a type of ALS that is inherited. Mutations in a protein called progranulin may also play a role in some TDP43-opathies.

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.

Clinically, FTD is classified into two main types of syndromes:

- *Behavioral variant frontotemporal dementia* 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.

- *Primary progressive aphasia (PPA)* 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.

Other types of FTDs include:

- *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.
- *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.

**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.

**Argyrophilic grain disease** is a common, late-onset degenerative disease characterized by tau deposits called argyrophilic grains in brain regions involved in memory and emotion. The disease's signs and symptoms are indistinguishable from late-onset AD. Confirmation of the diagnosis can be made only at autopsy.

## Synucleinopathies

In these brain disorders, a protein called alpha-synuclein accumulates inside neurons. Although it is not fully understood what role this protein plays, changes in the protein and/or its function have been linked to Parkinson's disease and other disorders.

One type of synucleinopathy, **Lewy body dementia**, involves protein aggregates called Lewy bodies, balloon-like structures that form inside of nerve cells. The initial symptoms may vary, but over time, people with these disorders develop very similar cognitive, behavioral, physical, and sleep-related symptoms. Lewy body dementia is one of the most common causes of dementia, after Alzheimer's disease and vascular disease. Types of Lewy body dementia include:

- *Dementia with Lewy bodies (DLB)*, 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)*, 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 nightmares and visual hallucinations.

## **Vascular Dementia and Vascular Cognitive Impairment**

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.

Some types of vascular dementia include:

**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, decisionmaking, 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.

## **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.

## **Other Conditions That Cause Dementia**

Doctors have identified many other conditions that can cause dementia or dementia-like symptoms.

### **Other Brain Diseases**

**Creutzfeldt-Jakob disease (CJD).** 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.” Inherited forms of CJD include:

- *Fatal familial insomnia*. This prion disease causes a part of the brain involved in sleep to slowly degenerate. People with the disease have trouble sleeping and may show signs of poor reflexes and hallucinations.
- *Gerstmann-Straussler-Scheinker disease*. Symptoms include a loss of coordination (ataxia) and dementia that begin when people are 50 to 60 years old.

**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 have a 50 percent chance of having the disorder.

**Secondary dementias.** These dementias occur in people with disorders that damage brain tissue. Such disorders may include multiple sclerosis; meningitis; encephalitis; and Wilson’s disease, in which excessive amounts of copper build up to cause brain damage. In rare cases, people with brain tumors may develop dementia because of damage to their brain circuits or a buildup of pressure inside the skull. Symptoms may include changes in personality, psychotic episodes, or problems with speech, language, thinking, and memory.

## Head Injury

**Chronic traumatic encephalopathy**, initially known as dementia pugilistica, 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.

**Subdural hematoma**, or bleeding between the brain’s surface and its outer covering (the dura), is common in the elderly after a fall. Subdural hematomas can cause dementia-like symptoms and changes in mental function. With treatment, some symptoms can be reversed.

## Reversible Dementias

Many conditions that cause dementia can be reversed with the appropriate treatment.

- Cerebral vasculitis, an inflammation and necrosis (tissue death) of blood vessel walls, can cause a form of dementia that may resolve when the person is treated with immune suppressants.
- Some studies have shown that people with depression are at increased risk of developing dementia. Severe depression can cause dementia and can be treated.
- Infections can cause confusion or delirium due to related fever or other side effects associated with the body's response to a foreign entity.
- Metabolic disorders of the nervous system, such as mitochondrial disorders, leukodystrophies, and lysosomal storage diseases, can lead to dementia.
- Metabolic problems and endocrine abnormalities such as thyroid problems, low blood sugar levels (called hypoglycemia), and low or high levels of sodium or calcium also may also cause dementia.
- Normal pressure hydrocephalus is an abnormal buildup of cerebro- spinal fluid in the brain. Elderly individuals with the condition usually have trouble with walking and bladder control before onset of dementia. Normal pressure hydrocephalus can be treated or even reversed by implanting a shunt system to divert fluid from the brain.
- Nutritional deficiencies of vitamin B<sub>1</sub> (thiamine), caused by chronic alcoholism, and vitamin B<sub>12</sub> deficiencies can be reversed with treatment.
- Paraneoplastic syndromes (a group of symptoms that may develop when substances released by some cancer cells disrupt the normal function of surrounding cells and tissue) can cause symptoms that resemble dementia. Such symptoms generally occur in people with cancer when the body's immune response to the cancer also ends up targeting proteins in the central nervous system. In many cases, the neurologic condition occurs before the cancer is detected. Circulating antibodies against brain proteins are common in both neurologic and cancer conditions.
- Side effects of medications or drug combinations may cause dementias that arise quickly or develop slowly over time.

## Causes

### Environmental Factors

Environmental factors may play a role in the development of certain types of dementia. This relationship is complex, however, since a person may carry genetic mutations that influence his or her response to environmental factors. Examples of environmental factors include:

**Anoxia.** Anoxia and a related condition, hypoxia, are terms often used to describe a state in which there is a curtailed supply of oxygen to an organ's tissues. Anoxia and hypoxia can lead to the loss of neurons and diffuse brain injury. Characteristics of the resulting dementia include confusion, personality changes, hallucinations, or memory loss. This type of dementia commonly occurs in people who survive cardiac arrest.

**Poisoning.** Exposure to lead, mercury, other heavy metals, or poisonous substances can lead to symptoms of dementia. These symptoms may or may not resolve after treatment, depending on how severely the brain is damaged.

**Substance abuse.** People who have abused substances such as alcohol and recreational drugs sometimes display signs of dementia even after the substance abuse has stopped. This condition is known as substance- induced persisting dementia.

## **Infectious Disease**

**HIV-associated dementia (HAD)** can occur in people who are positive for the human immunodeficiency virus, the virus that causes AIDS. HAD damages the brain's white matter and leads to a type of dementia associated with memory problems, social withdrawal, and trouble concentrating. People with HAD may develop movement problems as well. The incidence of HAD has dropped dramatically with the availability of effective antiviral therapies for managing the underlying HIV infection.

## **Risk Factors for Dementia**

The following risk factors can increase a person's chance of developing one or more kinds of dementia. Some of these factors can be modified, while others cannot.

- **Age.** The risk goes up with advanced age.
- **Alcohol use.** Most studies suggest that drinking large amounts of alcohol increases the risk of dementia, while drinking a moderate amount may be protective.
- **Atherosclerosis.** The accumulation of fats and cholesterol in the lining of arteries, coupled with an inflammatory process that leads to a thickening of the vessel walls (known as atherosclerosis), can hinder blood from getting to the brain, which can lead to stroke or another brain injury. For example, high levels of low-density lipoprotein (LDL, or "bad" cholesterol) can raise the risk for vascular dementia. High LDL levels also have been linked to AD.
- **Diabetes.** People with diabetes appear to have a higher risk for dementia, although the evidence for this association is modest. Poorly controlled diabetes, however, is a well-proven risk factor for stroke and cardiovascular disease-related events, which in turn increase the risk for vascular dementia.
- **Down syndrome.** Many people with Down syndrome develop early- onset AD, with signs of dementia by the time they reach middle age.
- **Genetics.** One's likelihood of developing a genetically linked form of dementia increases when more than one family member has the disorder. But in some cases, such as with CADASIL, having just one parent who carries a mutation increases the risk of inheriting the condition. In other instances, genetic mutations may underlie dementias in specific populations. For example, a mutation of the gene TREM2 has been found to be common among people with a form of very early onset frontotemporal dementia that runs in Turkish families.
- **Hypertension.** High blood pressure has been linked to cognitive decline, stroke, and types of dementia that affect the white matter regions of the brain.
- **Mental illness.** Depression has been associated with mild mental impairment and cognitive function decline.

- **Smoking.** Smokers are prone to diseases that slow or stop blood from getting to the brain.

## Diagnosing

Doctors first assess whether the individual has an underlying treatable condition such as depression, abnormal thyroid function, drug-induced encephalopathy, normal pressure hydrocephalus, or vitamin B<sub>12</sub> deficiency. Early diagnosis is important, as some causes for symptoms can be treated. In many cases, the specific type of dementia that a person has may not be confirmed until after the person has died and the brain is examined.

An assessment generally includes:

- **Patient history.** Typical questions about a person's medical and family history might include asking about whether dementia runs in the family, how and when symptoms began, and if the person is taking certain medications that might cause or exacerbate symptoms.
- **Physical exam.** Measuring blood pressure and other vital signs may help physicians detect conditions that might cause or occur with dementia. Such conditions may be treatable.
- **Neurological evaluations.** Assessing balance, sensory function, reflexes, vision, eye movements, and other functions helps identify signs of conditions that may affect the diagnosis or are treatable with drugs. Doctors also might use an electroencephalogram, a test that records patterns of electrical activity in the brain, to check for abnormal electrical brain activity.

The following procedures also may be used when diagnosing dementia:

- **Brain scans.** These tests can identify strokes, tumors, and other problems that can cause dementia. Scans also identify changes in the brain's structure and function. The most common scans are computed tomographic (CT) scans and magnetic resonance imaging (MRI). CT scans use X-rays to produce images of the brain and other organs. MRI scans use a computer, magnetic fields, and radio waves to produce detailed images of body structures, including tissues, organs, bones, and nerves.
- Other types of scans let doctors watch the brain as it functions. Two of these tests are single photon-emission computed tomography, which can be used to measure blood flow to the brain, and positron emission tomography (PET), which uses radioactive isotopes to provide pictures of brain activity. These scans are used to look for patterns of altered brain activity that are common in dementia. Researchers also use PET imaging with compounds that bind to beta-amyloid to detect levels of the protein, a hallmark of AD, in the living brain.
- **Cognitive and neuropsychological tests.** These tests measure memory, language skills, math skills, and other abilities related to mental functioning. For example, people with AD often show impairment in problem-solving, memory, and the ability to perform once-automatic tasks.

- **Laboratory tests.** Many tests help rule out other conditions. They include measuring levels of sodium and other electrolytes in the blood, a complete blood count, a blood sugar test, urine analysis, a check of vitamin B12 levels, cerebrospinal fluid analysis, drug and alcohol tests, and an analysis of thyroid function.
- **Presymptomatic tests.** Some dementias are associated with a known gene defect. In these cases, a genetic test could help people know if they are at risk for dementia. People should talk with family members, their primary health care professional, and a genetic counselor before getting tested.
- **Psychiatric evaluation.** This will help determine if depression or another mental health condition is causing or contributing to a person's symptoms.

## Treatment

Some dementias are treatable. However, therapies to stop or slow common neurodegenerative diseases such as AD have largely been unsuccessful, though some drugs are available to manage certain symptoms.

Most drugs for dementia are used to treat symptoms in AD. One class of drugs, called cholinesterase inhibitors, includes donepezil, rivastigmine, and galantamine. These drugs can temporarily improve or stabilize memory and thinking skills in some people by increasing the activity of the cholinergic brain network. The drug memantine is in another class of medications called NMDA receptor antagonists, which prevents declines in learning and memory. NMDA receptor antagonists work by regulating the activity of the neurotransmitter glutamate. When glutamate activity levels are excessive, neurons may die. Memantine may be combined with a cholinesterase inhibitor for added benefits. These drugs are sometimes used to treat other dementias as well. None of these drugs can stop or reverse the course of the disease.

- **Creutzfeldt-Jakob disease.** There are no treatments to cure or control CJD. Management focuses on reducing symptoms and making people comfortable.
- **Dementia with Lewy bodies.** Drugs available for managing DLB are aimed at relieving symptoms such as stiffness, hallucinations, and delusions. However, many of the agents for treating the physical symptoms, particularly antipsychotics, can make the mental health symptoms worse. Conversely, drugs used to treat mental health symptoms can exacerbate physical symptoms. Studies suggest that AD drugs may benefit people with DLB.
- **Frontotemporal disorders.** There are no medications approved to treat or prevent FTD and most other types of progressive dementia. Sedatives, antidepressants, and other drugs used to treat Parkinson's and Alzheimer's symptoms may help manage certain symptoms and behavioral problems associated with the disorders.
- **Parkinson's disease dementia.** Some studies suggest that the cholinesterase inhibitors used in people with AD might improve cognitive, behavioral, and psychotic symptoms in people with Parkinson's disease dementia. The U.S. Food and Drug Administration has approved one Alzheimer's drug, rivastigmine, to treat cognitive symptoms in PDD.

- **Vascular dementia.** This type of dementia is often managed with drugs to prevent strokes. The aim is to reduce the risk of additional brain damage. Some studies suggest that drugs that improve memory in AD might benefit people with early vascular dementia. Most of the modifiable risk factors that influence development of vascular dementia and VCI are the same risk factors for cerebrovascular disease, such as hypertension, atrial fibrillation, diabetes, and high cholesterol. Interventions that address these risk factors may be incorporated into the management of vascular dementia.

## Current Research

In 2012, the President announced the National Plan to Address Alzheimer’s Disease, a national effort to expand research in Alzheimer’s and related dementias prevention and treatment and to move the most promising drugs from discovery into clinical trials. The Plan aims to prevent and effectively treat Alzheimer’s and related dementias by 2025. Its foundation is the 2011 National Alzheimer’s Project Act (NAPA), which was developed to create and maintain a national strategy to overcome the disease. The National Plan calls for increased federal funding for AD research, support for those affected by AD and their families, increased public awareness about AD, and improved data collection and analysis to better understand the impact of AD on people with the disease, families, and the health and long-term care systems. These goals also apply to AD-related dementias, including dementia with Lewy bodies as well as frontotemporal, mixed (characteristics of more than one type of dementia occur simultaneously), and vascular dementias. For more information, see <http://aspe.hhs.gov/daltcp/napa/NatlPlan.pdf>.

The National Institute of Neurological Disorders and Stroke (NINDS), a component of NIH, is the leading federal funder of research on nervous system disorders. Another NIH Institute, the National Institute on Aging (NIA), is the leading federal funder of research on AD. Together, these Institutes are world leaders in supporting research on the dementias, including Lewy body dementia, frontotemporal disorders, and vascular dementia.

Although scientists have some understanding of these dementias and the mechanisms involved, ongoing research may lead to new ways to diagnose, treat, or perhaps prevent or block disease development. Current areas of research include:

**Clinical studies.** Clinical studies offer an opportunity to help researchers find better ways to safely detect, treat, or prevent dementias. Various NIH Institutes support clinical studies on AD and related dementias at the NIH research campus in Bethesda, MD, and at medical research centers throughout the U.S. For information about participating in clinical studies for AD, related dementias, and other disorders, visit “NIH Clinical Research Trials and You” at [www.nih.gov/health/clinicaltrials](http://www.nih.gov/health/clinicaltrials). For a list of AD clinical trials and studies, see [www.nia.nih.gov/alzheimers/clinical-trials](http://www.nia.nih.gov/alzheimers/clinical-trials). For a comprehensive list of all trials, go to [www.clinicaltrials.gov](http://www.clinicaltrials.gov).

**Drugs.** A number of agents that might slow the progression of AD and other dementias are in various stages of testing.

The NIA-supported Alzheimer's Disease Cooperative Study (ADCS) ([www.adcs.org](http://www.adcs.org)) is a consortium of academic medical centers and clinics set up by NIH in 1991 to collaborate on the development of promising Alzheimer's treatments and diagnostic tools.

In the latest round of studies, the ADCS will test drug and exercise interventions in people in the early stages of the disease, examine a medication to reduce agitation in people with Alzheimer's dementia, and test a cutting-edge approach to speed testing of drugs in clinical trials. Because Alzheimer's-related brain changes begin years before symptoms appear, the A4 (Anti-amyloid Treatment in Asymptomatic Alzheimer's Disease) trial is testing a promising therapy in the early stages of the disorder. This secondary prevention trial will test an amyloid-clearing drug in the symptom-free stage of the disease in 1,000 cognitively healthy older volunteers whose brain scans show abnormal levels of amyloid accumulation. Another of the newly funded ADCS drug trials is the Prazosin for Treating Agitation trial, which will test the use of the generic drug prazosin as a treatment for agitation that may also be well-tolerated in frail and elderly people.

**Exercise.** Researchers are assessing the effectiveness of a supervised aerobic exercise program to enhance general cognition in adults with age-related cognitive decline. They predict that greater cognitive gains will be made by individuals with more fitness gains. Another study will determine if exercise prevents memory loss from getting worse, and if it improves daily functioning and attitudes of those with probable AD. Researchers also hope to gain a better understanding of the effects of exercise and cognitive training on improving brain function in healthy older adults who may be at risk for developing AD.

**Genetics.** Several genes—most notably ApoE and the gene for tau (MAPT)—have been implicated in AD and other forms of dementia. Many dementia-related disorders share genetic and other characteristics of AD. Some families share a particular genetic mutation that causes dementia. Researchers are using samples of a person's genetic material, or genome, to identify genes that may be responsible for the development of dementia and AD. For example, NIH-funded researchers recently examined ApoE's role in the development of late-onset AD and found that one of the three forms of the ApoE gene triggers an inflammatory reaction and damages the blood vessels that feed the brain. Other researchers have identified a gene variant of TREM2 that is involved with a form of frontotemporal dementia that runs in families. Additional research may identify novel genes involved with FTD and other neurodegenerative diseases, perhaps leading to therapeutic approaches where delivery of normal genes would improve or restore normal brain function.

**Imaging.** Clinical imaging may help researchers better understand changes in the brains of people with dementia, as well as help diagnose these disorders. Magnetic resonance imaging may reveal structural and functional differences in the brains of individuals with Parkinson's disease dementia and AD and identify small vessel disease. PET scanning uses ligands—radioactive molecules that bind to proteins to show chemical functions of tissues and organs in the body—to help produce images of brain activity. Scientists funded by NIA are testing new PET ligands that bind to beta-amyloid for early detection of Alzheimer's-type pathology and cognitive decline. Studies of PET ligands that bind to aggregates of tau are ongoing in people with very early-stage AD.

**International efforts.** The International Alzheimer’s Disease Research Portfolio (IADRP) helps individuals learn about AD research at public and private organizations in the U.S. and abroad. It also helps organizations leverage resources and avoid duplication of effort. The Common Alzheimer’s Disease Research Ontology—a classification system that allows organizations to integrate and compare research portfolios—was developed by NIA, NIH, and the Alzheimer’s Association. For more information about IADRP, see <http://iadrp.nia.nih.gov/cadro-web/about>.

**Proteins.** One feature that several major dementias have in common is an excess in the brain of certain proteins or protein fragments that have taken abnormal forms thought to be toxic to brain cells. NIH-funded research projects are aimed at better understanding the toxic effects of protein buildup and how it is related to the development of AD and related dementias. Some of these protein abnormalities can be detected in cerebrospinal fluid.

For example, an abnormally high accumulation of beta-amyloid protein in the brain is a hallmark of AD. NINDS-funded researchers are determining which neural pathways are affected by beta-amyloid and contribute to the development of Alzheimer’s pathology and symptoms. NINDS funding also led to a genetically engineered rat model of AD that has the full array of brain changes associated with the human disease and may be used to better define causes and effects of AD related to beta-amyloid accumulation. Funding also was provided by NIA, the National Institute of Mental Health (also part of NIH), and other organizations.

In FTD, AD, and other neurodegenerative diseases, the protein tau collects in abnormal tangled masses of filaments that disrupt nerve signaling, cause cell death, and impair cognition. NINDS-funded researchers are determining whether specific forms of tau interfere with nerve cell signaling and decrease memory function. Others are studying how tau pathology spreads from cell to cell. Tau-related investigations are aimed at identifying common mechanisms of FTD, as well as biomarkers (signs that may indicate disease risk and progression, and improve diagnosis) that will speed the development of novel therapeutics for PDD and other forms of dementia.

Similarly, the abnormal accumulation of the protein alpha-synuclein is a hallmark of Parkinson’s disease and Lewy body dementia. Scientists hope to identify what causes alpha-synuclein to form abnormal aggregates and become toxic to nerve cells, and to understand why the aggregation is an age-related phenomenon in Parkinson’s disease and other synuclein-related disorders.

**Sleep.** The sleep and wakefulness cycle plays an integral, but not well understood, role in many dementias, including dementia with Lewy bodies, AD, prion dementias, and PDD. Sleep studies in individuals during periods of excessive daytime sleepiness and nocturnal sleep can help determine if fluctuations in mental status among people with DLB are related to excessive daytime sleepiness. Sleep studies also can assess whether declining cognition is predicted by sleep-related and neurobehavioral markers in parkinsonism.

**Stem cells.** Scientists are exploring various types of cells, including stem cells, to discover nerve cell mechanisms that lead to the initiation and progression of AD and other forms of dementia. Significant research efforts have focused on induced pluripotent stem cells (iPSC), which can be “reprogrammed” from skin cells into any cell type in the body, including nerve cells. NINDS

funds three research consortia to develop well-characterized iPSC for amyotrophic lateral sclerosis (ALS), Huntington's disease, and Parkinson's disease. These cells can then be used by the research community to study the effects of mutant genes and misfolded proteins on nerve cell function and health, as well as to test potential drugs and therapies for AD and related dementias.

## **Conclusion**

Currently, there are no cures for the common dementias caused by progressive neurodegeneration, including AD, frontotemporal disorders, and Lewy body dementia. However, some forms of dementia are treatable. A better understanding of dementia disorders, as well as their diagnosis and treatment, will make it possible for affected individuals and their caretakers to live their lives more fully and meet daily challenges. NIH, primarily through research activities funded by NINDS and NIA, continues to make discoveries in the lab, design therapeutic approaches to dementias, and create tools and resources to help speed the development of treatments that can be used in practice. These discoveries may eventually lead to ways to slow disease progression or even cure and prevent the dementias.

## **THERAPEUTIC RECREATION<sup>8</sup>**

Recreation, play or work, no matter what word is used to describe activity, activities are an essential part of an individual's life. From an early age children play. This early stage of play has no structure, but it is vital for the child's social and intellectual development. Sulva, K. Lunt, I. (1982).

In adult life meaningful activities are just as vital as this early type of play to prevent boredom, isolation and aggression. Roper et al (1988). Throughout adult life we spend most of our time working to provide ourselves and family with shelter, warmth and food. Groenman, N. H. D'A Slevin, O. Buckenham, M. A. (1992). But alongside work we also need to relax.

This is achieved in many different forms which may be in isolation, or in groups of various sizes depending on the individual needs and activity involved. In the well adult this can be easily achieved by the individual themselves. Though in the sick this need for leisure activities can cause concern for individuals and may well prevent the individuals from having a meaningful life style which may ultimately affect recovery.

In latter years, the needs pertaining to leisure requirements in the elderly have been addressed by many businesses such as banks, by encouraging the individual to plan for retirement and providing courses to deal with the prospect of retirement.

## RESOURCES

For more information on neurological disorders or research programs funded by the National Institute of Neurological Disorders and Stroke, contact the Institute's Brain Resources and Information Network (BRAIN) at:

BRAIN

P.O. Box 5801

Bethesda, MD 20824

(800) 352-9424

<http://www.ninds.nih.gov>

Information also is available from the following organizations:

<p><b><u><a href="#">Alzheimer's Disease Education and Referral Center (ADEAR)</a></u></b>  <b><u><a href="#">National Institute on Aging</a></u></b>            P.O. Box 8250            Silver Spring, MD 20907-8250  <b><a href="mailto:adear@nia.nih.gov">adear@nia.nih.gov</a></b>  <b><u><a href="http://www.nia.nih.gov/alzheimers">http://www.nia.nih.gov/alzheimers</a></u></b>            Tel: 1-800-438-4380            Fax: 301-495-3334</p>	<p><b><u><a href="#">Alzheimer's Association</a></u></b>            225 North Michigan Avenue            Floor 17            Chicago, IL 60601-7633  <b><a href="mailto:info@alz.org">info@alz.org</a></b>  <b><u><a href="http://www.alz.org">http://www.alz.org</a></u></b>             Tel: 312-335-8700 1-800-272-3900 (24-hour helpline) TDD: 312-335-5886            Fax: 866.699.1246</p>
<p><b><u><a href="#">Alzheimer's Foundation of America</a></u></b>            322 Eighth Avenue            7th Floor            New York, NY 10001  <b><a href="mailto:info@alzfdn.org">info@alzfdn.org</a></b>  <b><u><a href="http://www.alzfdn.org">http://www.alzfdn.org</a></u></b>             Tel: 866-AFA-8484 (232-8484)            Fax: 646-638-1546</p>	<p><b><u><a href="#">Alzheimer's Drug Discovery Foundation</a></u></b>            57 West 57th Street            Suite 904            New York, NY 10019  <b><a href="mailto:info@alzdiscovery.org">info@alzdiscovery.org</a></b>  <b><u><a href="http://www.alzdiscovery.org">http://www.alzdiscovery.org</a></u></b>             Tel: 212-901-8000            Fax: 212-901-8010</p>
<p><b><u><a href="#">Association for Frontotemporal Degeneration (AFTD)</a></u></b>            Radnor Station Building #2 Suite 320            290 King of Prussia Road            Radnor, PA 19087  <b><a href="mailto:info@theaftd.org">info@theaftd.org</a></b>  <b><u><a href="http://www.theaftd.org">http://www.theaftd.org</a></u></b>             Tel: 267-514-7221 866-507-7222</p>	<p><b><u><a href="#">BrightFocus Foundation</a></u></b>            22512 Gateway Center Drive            Clarksburg, MD 20871  <b><a href="mailto:info@brightfocus.org">info@brightfocus.org</a></b>  <b><u><a href="http://www.brightfocus.org/alzheimers/">http://www.brightfocus.org/alzheimers/</a></u></b>             Tel: 1-800-437-2423            Fax: 301-258-9454</p>

<p><b><u><a href="#">John Douglas French Alzheimer's Foundation</a></u></b>  11620 Wilshire Blvd.  Suite 270  Los Angeles, CA 90025  <a href="http://www.jdfaf.org">http://www.jdfaf.org</a>  Tel: 310-445-4650  Fax: 310-479-0516</p>	<p><b><u><a href="#">Lewy Body Dementia Association</a></u></b>  912 Killian Hill Road, S.W.  Lilburn, GA 30047  <b><a href="mailto:lbda@lbda.org">lbda@lbda.org</a></b>  <a href="http://www.lbda.org">http://www.lbda.org</a>  Tel: Telephone: 404-935-6444 LBD Caregiver  Link: 800-539-9767  Fax: 480-422-5434</p>
<p><b><u><a href="#">National Institute of Mental Health (NIMH)</a></u></b>  National Institutes of Health, DHHS  6001 Executive Blvd. Rm. 8184, MSC  9663  Bethesda, MD 20892-9663  <b><a href="mailto:nimhinfo@nih.gov">nimhinfo@nih.gov</a></b>  <a href="http://www.nimh.nih.gov">http://www.nimh.nih.gov</a>  Tel: 301-443-4513/866-415-8051 301-443-8431 (TTY)  Fax: 301-443-4279</p>	<p><b><u><a href="#">National Organization for Rare Disorders (NORD)</a></u></b>  55 Kenosia Avenue  Danbury, CT 06810  <b><a href="mailto:orphan@rarediseases.org">orphan@rarediseases.org</a></b>  <a href="http://www.rarediseases.org">http://www.rarediseases.org</a>  Tel: 203-744-0100 Voice Mail 800-999-NORD (6673)  Fax: 203-798-2291</p>

## Glossary

**Alpha-synuclein**—a protein that is implicated in abnormal clumps called Lewy bodies, which are seen in the brains of people with Parkinson’s disease and some dementias. Disorders in which alpha-synuclein accumulates inside nerve cells are called synucleinopathies.

**Alzheimer’s disease**—the most common cause of dementia in people age 65 and older. Nearly all brain functions, including memory, movement, language, judgment, and behavior, are eventually affected.

**Amyloid**—a protein found in the characteristic clumps of tissue (called plaques) that appear in the brains of people with Alzheimer’s disease.

**Chronic traumatic encephalopathy**—a form of dementia caused by repeated traumatic brain injury.

**Corticobasal degeneration**—a progressive disorder characterized by nerve cell loss and atrophy in multiple areas of the brain.

**Dementia**—a term for a collection of symptoms that significantly impair thinking and normal activities and relationships.

**Dementia with Lewy bodies**—a type of Lewy body dementia that is a common form of progressive dementia.

**Frontotemporal disorders**—a group of dementias characterized by degeneration of nerve cells, especially those in the frontal and temporal lobes of the brain.

**HIV-associated dementia**—a dementia that results from infection with the human immunodeficiency virus that causes AIDS.

**Lewy body dementia**—one of the most common types of progressive dementia, characterized by the presence of abnormal structures called Lewy bodies in the brain.

**Mixed dementia**—dementia in which one form of dementia and another condition or dementia cause damage to the brain, for example, Alzheimer's disease and small vessel disease or vascular dementia.

**Multi-infarct dementia**—a type of vascular dementia caused by numerous small strokes in the brain.

**Neurofibrillary tangles**—bundles of twisted filaments found in nerve cells in the brains of people with Alzheimer's disease. These tangles are largely made up of a protein called tau.

**Parkinson's disease dementia**—a secondary dementia that sometimes occurs in people with advanced Parkinson's disease. Many people with Parkinson's have the amyloid plaques and neurofibrillary tangles found in Alzheimer's disease, but it is not clear if the diseases are linked.

**Tau**—a protein that helps the functioning of microtubules, which are part of the cell's structural support and help deliver substances throughout the cell. In Alzheimer's disease, tau twists into filaments that become tangles. Disorders associated with an accumulation of tau, such as frontotemporal dementia, are called tauopathies.

**Vascular dementia**—a type of dementia caused by brain damage from cerebrovascular or cardiovascular problems, usually strokes.

"Dementia: Hope Through Research," NINDS

## REFERENCES

- 
- <sup>1</sup> <http://www.who.int/topics/disabilities/en/>
  - <sup>2</sup> <http://www.patient.co.uk/doctor/disability-in-older-people#ref-2>
  - <sup>3</sup> <http://report.nih.gov/nihfactsheets/ViewFactSheet.aspx?csid=37>
  - <sup>4</sup> <http://www.patient.co.uk/doctor/disability-in-older-people#ref-2>
  - <sup>5</sup> <http://www.nia.nih.gov/alzheimers>
  - <sup>6</sup> [http://www.pdf.org/about\\_pd](http://www.pdf.org/about_pd)
  - <sup>7</sup> [http://www.ninds.nih.gov/disorders/dementias/detail\\_dementia.htm#glossary](http://www.ninds.nih.gov/disorders/dementias/detail_dementia.htm#glossary)
  - <sup>8</sup> <http://www.recreationtherapy.com/re-elder.htm>