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When Alzheimer disease strikes early

Alzheimer disease is generally seen in individuals age 65 and older; however, in approximately 5% of cases, it occurs in those younger than age 65.

By Amanda Perkins, MSN, RN

A progressive, degenerative disease affecting the cerebral cortex—the site at which the highest level of neural processing takes place—Alzheimer disease in individuals younger than age 65 is termed early-onset. Typically affecting people between ages 40 and 50, early-onset Alzheimer disease may be seen in individuals as young as age 30.

Two types

There are two types of early-onset Alzheimer disease: common and genetic. Common Alzheimer disease is the type that occurs in most cases, whereas the genetic form of the disease is extremely rare. With genetic Alzheimer disease, signs and symptoms typically develop between ages 30 and 50.

The cause of common early-onset Alzheimer disease is unknown, whereas the genetic type is associated with a mutation in one of three genes located on three different chromosomes: 1, 14, and 21 (see *Genetics and early-onset Alzheimer disease*). The mutations seen on the chromosomes are as follows:

- chromosome 1—presenilin 2 (PSEN2)
- chromosome 14—presenilin 1 (PSEN1)
- chromosome 21—amyloid precursor protein (APP).

Presenilin proteins are linked to early-onset Alzheimer disease. The genes that code for them are found on chromosomes 1 and 2. Of the three mutations, PSEN1 and PSEN2 account for the majority of genetic early-onset Alzheimer disease cases (see *Mutant presenilin*). These genetic mutations shouldn't be confused with the apolipoprotein, or APOE, gene, which increases the overall risk of Alzheimer disease.

Research related to the correlation of Alzheimer disease with health, environment, and lifestyle factors is ongoing. It's believed that the disease may be linked with vascular conditions, such as heart disease, stroke, and

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hypertension, as well as metabolic conditions, such as diabetes and obesity.

Changes in the brain

Alzheimer disease is characterized by beta-amyloid plaques, neurofibrillary tangles, neuronal degeneration, and diffuse atrophy of the cerebral cortex.

Beta-amyloid plaques occur as the result of accumulation of beta-amyloid—a small fibrillary peptide that builds up in the spaces around synapses, the communication points between neurons. Beta-amyloid is a normal finding in healthy individuals. Under normal conditions, the beta-amyloid that's in the brain dissolves and is removed by the body.

In patients with Alzheimer disease, there's too much beta-amyloid present and the body isn't able to remove it, resulting in an accumulation of the peptide. The beta-amyloid accumulates into fibrils that clump together and form plaques that effectively kill brain cells, which causes a disruption in brain functioning. Although it's known that beta-amyloid causes brain cell death, it's unknown how this process occurs. Unlike other cells found in the body, brain cells can't be replaced once they die. As more brain cells die in the patient with Alzheimer disease, symptoms become increasingly pronounced.

It's believed that APP—the parent protein for beta-amyloid—plays a role in beta-amyloid plaque formation. APP is a large protein found in the brain, heart, kidneys, lungs, spleen, and intestines. It protrudes through the neuronal membrane, with a portion of the protein found within the cell and the remainder on the outside of the cell. Enzymes cut APP into two fragments, leaving a beta-amyloid fragment within the brain. It's known that once cut, the APP fragments clump together; however, it's unknown what exactly happens within the body to cause the clumping.

Neurofibrillary tangles are abnormal clumps of proteins, in some cases tau. Helping maintain nerve cell structure and making it possible for the cells to carry nutrients from the cell body to the axons, tau plays a critical role in the brain. In patients with Alzheimer disease, tau protein abnormally twists, causing axons to tangle and leading to the development of neurofibrillary tangles in neuronal cell bodies. The plaques and tangles that develop in the brain are found in areas important

Genetics and early-onset Alzheimer disease

Let's delve deeper into chromosomes and the abnormal genes found on chromosomes 1, 14, and 21. A chromosome is a structure found within cells; specifically, within the cell nucleus. Chromosomes are made up of tightly coiled strands of genes that are the blueprint for each individual person. We receive 23 chromosomes from each parent, for a total of 46 chromosomes. Mutations of the genes found on these chromosomes can lead to various diseases such as Alzheimer disease. Defects in the genes found on chromosomes 1, 14, and 21 have been associated with early-onset Alzheimer disease.

Chromosome 1

The gene mutation that occurs with chromosome 1 is found in the gene STM2, which codes for PSEN2. This abnormality is rare and seen most commonly in descendants of Germans who immigrated to Russia in the 18th century and then to the United States in the 20th century.

Chromosome 14

The gene mutation that occurs with chromosome 14 is found in the gene S182, which codes for PSEN1. This gene mutation is much more common, accounting for approximately 80% of all cases of inherited Alzheimer disease.

Chromosome 21

This chromosome is the smallest in the entire genome. The mutation that occurs with chromosome 21 is found in APP. Abnormalities in APP are also linked to Down syndrome. Research has shown that most individuals with Down syndrome will develop Alzheimer disease by age 60.

Mutations found within the genes described above appear to accelerate the formation of beta-amyloid and lead to the development of plaques. Additionally, the presenilins associated with chromosomes 1 and 14 appear to cause apoptosis, a natural process in which cells are programmed to self-destruct (sometimes referred to as cellular suicide). Normally, apoptosis is beneficial to the body, eliminating unnecessary cells and targeting cancer cells so that healthy tissue can be maintained. With Alzheimer disease, apoptosis eliminates cells that the body needs.

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for memory and intellectual functions. Additionally, a loss of connections occurs between neurons—the brain cells responsible for not only communicating with different parts of the brain, but also from the brain to the body.

Damage in the brain may start in the hippocampus—the area responsible for memory formation. It's believed that this damage begins a decade before signs and symptoms develop. Healthy neurons stop functioning and, eventually, connections are lost, neurons are unable to communicate with one another, and neuronal death occurs. As neurons continue to die and connections are lost, new areas of the brain become affected until there's widespread damage and atrophy.

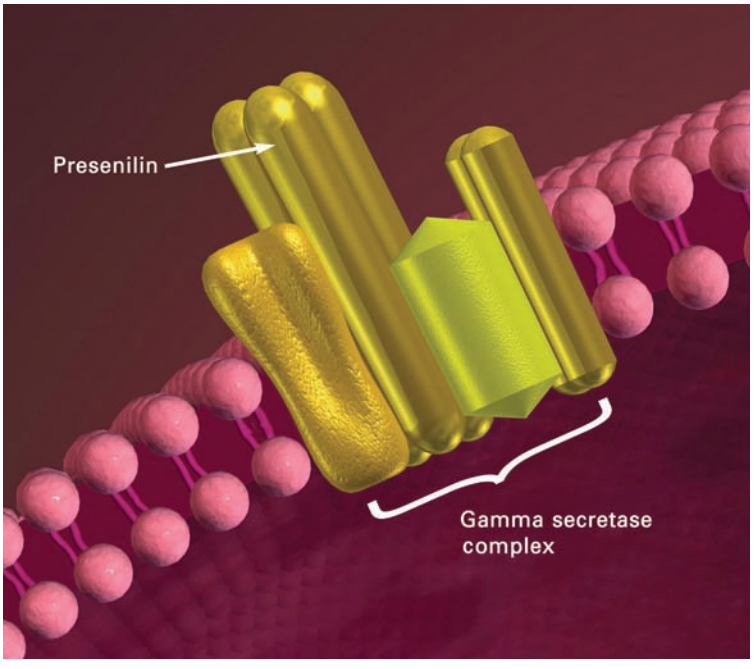
Research has indicated that individuals with early-onset Alzheimer disease may decline at a faster rate than those who develop Alzheimer disease after age 65. However, specific brain changes that occur before the development of symptoms haven't been demonstrated. The National Institute on Aging is currently conducting a study on early-onset Alzheimer disease. It's hoped that this study will be able to identify changes that occur before symptom development.

Signs and symptoms

The symptoms associated with early-onset Alzheimer disease are similar and overlap with those seen in other forms of the disease, including:

- early symptoms
  - –forgetfulness, especially with new information
  - –repeatedly asking the same questions
  - –difficulty solving basic problems
  - –losing track of the date and/or time of year
  - –losing track of location and how the person arrived at the location
  - –problems with depth perception
  - –difficulty with conversations
  - –difficulty with word finding
  - –difficulty concentrating
  - –misplacing items
  - –increasingly poor judgment
  - –withdrawal from work and/or social situations
  - –change in mood and personality
  - –increasing difficulty completing familiar tasks
  - –repeating stories
  - –forgetting names of familiar people
  - –wandering, especially at night
- late symptoms
  - –depression
  - –severe mood swings and behavior changes
  - –increasing agitation and irritability
  - –increasing confusion about time, place, and events
  - –suspicions about family and friends
  - –disinhibition

Mutant presenilin



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Mutations in the presenilin proteins (PSEN1 and PSEN2) and APP can be found in patients with early-onset Alzheimer disease (autosomal dominant hereditary). An important part of the disease process is the accumulation of beta-amyloid. To form it, APP must be cut by two enzymes: beta secretase and gamma secretase. Presenilin is the subcomponent of gamma secretase that's responsible for cutting APP.

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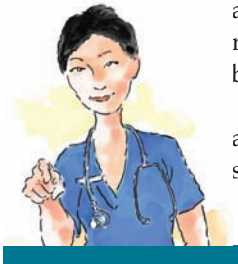
–difficulty speaking, swallowing, and walking
–severe memory loss
–psychosis
–incapacity for self-care.

Alzheimer disease is characterized by three different stages: mild, moderate, and severe. In the mild stage, the patient begins to have memory loss and cognitive difficulties. The patient and/or family members may report wandering, getting lost, having difficulty with money/paying bills, repeating questions, increasing difficulty with daily tasks, and personality and behavioral changes.

In the moderate stage, damage in the brain has spread to the areas responsible for language, sensory processes, conscious thought, and reasoning. In this stage, the patient may have increased memory loss and confusion, along with difficulty recognizing friends and family, learning new things, and performing complex tasks. The patient may also experience problems coping with new situations, hallucinations, delusions, paranoia, and impulsive behaviors.

In the severe stage, plaques and tangles are spread throughout the brain and brain atrophy is present. The patient will be bedridden and unable to communicate; the body will eventually shut down.

The progression of Alzheimer disease affects each individual differently. In some cases, the patient with early-onset Alzheimer disease may move through the stages more quickly. However, it's important to remember that each patient will progress through the stages at different speeds.



did you know?

Of the top 10 diseases causing death in the United States, Alzheimer disease is the only one that can't be prevented, cured, or slowed, according to the Alzheimer's Association. Occurring more commonly in female patients (two-thirds of those diagnosed), Alzheimer disease is very costly for patients, families, and the nation. According to the Alzheimer's Association, it's estimated that in 2015, the national cost of Alzheimer disease, as well as other dementias, was $226 billion. Additionally, it's estimated that without a cure or improved treatments, the cost will increase to $1.1 trillion by 2050.

Diagnosis

The diagnosis of early-onset Alzheimer disease can be challenging, with misdiagnosis occurring more commonly than with other types of the disease. Definitive diagnosis of Alzheimer disease can only be made after death when an autopsy can be completed. Diagnosis is based on a history and physical; signs and symptoms; cognitive tests; blood, urine, and spinal fluid analysis; and computed tomography (CT) or magnetic resonance imaging (MRI).

The cognitive tests conducted are used to assess memory, problem solving, and other mental skills. Many of these tests are performed serially so that changes in cognition and memory can be assessed. In addition, the patient's family and/or caregivers are asked about changes they've noticed. In many cases, the family and/or caregivers may be able to detect changes in the patient early on. CT and/or MRI may be utilized to assess damaged areas in the brain.

The usefulness of biologic markers, such as proteins and genes, is being researched. It's hoped that current research will lead to markers that can detect Alzheimer disease. If discovered, biomarkers specific to Alzheimer disease can be used to not only aid in diagnosis, but also predict future disease. At this time, CT and MRI are being researched as potential biomarkers for Alzheimer disease. These scans may prove useful by detecting brain shrinkage and slowed brain metabolism and blood flow.

At this time, individuals can be tested for the genetic mutations associated with Alzheimer disease, but this testing is typically limited to those with a family history.

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consider this

A 45-year old female patient arrives at the physician's office with complaints of increasing forgetfulness. She states that she started to have problems recalling names and dates approximately 6 months ago. She also reports that she has been having difficulty with word finding, concentrating, finding common household objects, and sleeping, along with mood swings. She tells you that she's concerned because her grandmother developed dementia at an early age.

Complications

Most of the complications seen with Alzheimer disease are those that arise from immobility, including:

- aspiration
- pneumonia and other infections
- falls
- fractures
- skin breakdown, such as pressure ulcers
- malnutrition and dehydration.

Aspiration occurs when patients inhale food and/or fluids into their lungs. As Alzheimer disease progresses, patients have increasing difficulty coordinating swallowing and breathing, leading to aspiration risk. If aspiration occurs, the patient may develop an infection, most commonly pneumonia.

The patient with Alzheimer disease has a high risk of falls due to increasing immobility, wandering, and poor safety awareness. Falls may raise the risk of fractures, which can be particularly dangerous for patients with Alzheimer disease because of the complications associated with immobility.

Patients with Alzheimer disease are also at risk for skin breakdown, specifically pressure ulcers, which lead to ischemia and potential tissue necrosis. As the patient becomes increasingly immobile, the risk of pressure ulcer development is higher.

In the advanced stages of Alzheimer disease, patients have increasing difficulty eating and drinking, leading to malnutrition and dehydration. Many patients don't die as a result of Alzheimer disease; rather, they die from pneumonia or other complications of immobility.

Although the complications associated with early-onset Alzheimer disease are the same as those seen in other Alzheimer patients, it's important to be aware that these complications can be particularly challenging for patients who develop the disease early, at a time in their life when they would normally be able to care for themselves and others. Family members may find it particularly difficult when a young spouse or parent is unable to eat independently, falls frequently, or experiences nighttime wandering.

Management

Alzheimer disease is a progressive disease that has no cure. Current treatment is aimed at helping patients maintain mental and physical function, control behavior, improve quality of life, and slow disease progression. Although treatment hasn't been shown to dramatically slow the progression of the disease, it's beneficial in controlling agitation, anxiety, behavioral problems, sleep disturbances, and depression. Treatment is most effective when started early.

It's important to be aware that, in most cases, medication is ineffective as the disease progresses. Medications, such as donepezil, rivastigmine, and memantine, may help slow the progression of the disease, but may only be beneficial for a few months to a few years.

Used to treat all stages of Alzheimer disease, donepezil works by increasing acetylcholine levels in the brain. For some patients, this medication improves thinking, overall function, and behavior. It isn't curative but, in some patients, it may slow disease progression. Donepezil is most effective when started early and becomes less effective as the disease progresses.

Used to treat mild-to-moderate Alzheimer disease, rivastigmine increases acetylcholine in the brain by blocking the enzymes that break it down. For some patients, this medication may improve thinking, remembering, the ability to

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perform activities of daily living (ADLs), and overall functioning.

When administering donepezil or rivastigmine, monitor the patient closely for interactions with other medications, such as antipsychotics, antiarrhythmics, beta-blockers, digoxin, and nonsteroidal anti-inflammatory drugs (NSAIDs). When given with antipsychotics, these medications can increase the risk of Parkinson-like symptoms. When given with antiarrhythmics, beta-blockers, and/or digoxin, they can cause bradycardia or other cardiac conduction problems. When given with NSAIDs, these medications can increase the risk of stomach ulcer development. Donepezil and rivastigmine are both cholinesterase inhibitors, meaning that they interfere with the breakdown of acetylcholine. They lose effectiveness as an increasing number of acetylcholine-producing cells die.

Memantine is a glutamate receptor-blocking agent used to treat moderate-to-severe Alzheimer disease. This medication regulates glutamate by blocking its action at receptors, which is important because these receptors are overstimulated in patients with Alzheimer disease. It may slow the progression of the disease, improve cognitive and psychomotor function, and improve the patient's ability to carry out ADLs. Memantine and the cholinesterase inhibitors act differently in the body and, as a result, can be administered together.

In addition to medications, the following may help delay disease progression:

- physical activity
- cardiovascular treatment
- diabetes treatment
- antioxidants
- cognitive training.

Research on the effectiveness of alternative treatments, such as light therapy, music therapy, pet therapy, and aromatherapy, is being conducted. Nonpharmacologic approaches are sought because they may be more cost effective and potentially decrease the amount of medications needed.

The treatment of early-onset Alzheimer disease mirrors that of other patients with Alzheimer disease. Treatment is aimed at slowing disease progression and allowing the patient to maintain independence for as long as possible. In some instances, the patient with early-onset Alzheimer disease may choose to participate in clinical trials.

Your role

Alzheimer disease can be a devastating diagnosis for your patients and they may need a great deal of emotional support. When caring for those with early-onset Alzheimer disease, be aware of your patients' stress levels and help them cope effectively. Always maintain a positive attitude when working with these patients and let them know that they aren't alone.

Provide education to patients and their families about the disease; legal documents, such as advance directives and living wills; and therapeutic interventions, including pharmacologic and nonpharmacologic approaches to care. If patients or their families are considering nonpharmacologic interventions, give them evidence-based information and encourage them to check with the healthcare provider before trying anything that they've seen on TV or researched on the Internet.

Encourage patients to stay mentally engaged and physically active for as long as they can. You'll also want to encourage them to plan ahead. Finances can be of particular concern because patients may need to stop working earlier than planned and experience a loss of income as a result. Additionally, the patient's spouse may need to quit his

did you know?

Medications selected for the treatment of Alzheimer disease include those that prevent the breakdown of acetylcholine, a chemical important for memory and thinking, and those that regulate glutamate, a brain chemical that can cause cell death when produced in large amounts. These medications are utilized because destruction occurring in the brain leads to decreased levels of acetylcholine and increased levels of glutamate, which can be neurotoxic and intensify signs and symptoms.

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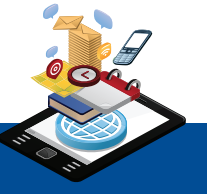
or her job, or cut back on hours to take on the caregiver role.

When caring for patients with Alzheimer disease, remember that these patients are sensitive to external stimuli and have a tendency to become easily agitated. Additionally, nighttime awakening is very common, which can create safety risks for the patient and cause caregiver strain. In many cases, individuals with early-onset Alzheimer disease will be living at home with family. Frequent awakenings and wandering at night can put stress on family members.

It's important to keep the patient's environment familiar and free of clutter, with minimal stimulation, good lighting, and an appropriate temperature. To create a familiar environment when the patient isn't at home, pictures and personal effects from home can be brought to the care facility. It may also be beneficial to provide consistent caregivers whenever possible and maintain a routine.

Alzheimer disease doesn't just affect an individual; rather, it changes the entire family dynamic and affects the family as a whole. Caregivers undergo great emotional stress, with 60% of people caring for patients with Alzheimer disease rating their stress levels as high to very high, according to the Alzheimer's Association. In addition to high stress levels, 40% of caregivers report that they experience depression. Many caregivers become stressed due to lack of support, minimal knowledge of available support services, and feeling unprepared for the care that needs to be provided.

This diagnosis can be particularly devastating for children who may have to take on the role of caregiver for a young parent and also be concerned about the possibility of developing early-onset Alzheimer disease themselves. Educate the children of patients with early-onset Alzheimer disease about genetic testing, but stress that it's a choice requiring careful consideration. Also be aware that this diagnosis can be very difficult for spouses who have to change their expectations of the future and take on a caregiving role for the person with whom they're sharing their life.



on the web

Alzheimer's Association:
www.alz.org/alzheimers_disease_early_onset.asp

John's Hopkins Medicine:
www.hopkinsmedicine.org/healthlibrary/conditions/nervous_system_disorders/early-onset_alzheimers_disease_134,63/

Mayo Clinic:
www.mayoclinic.org/alzheimers/art-20048356

National Institute on Aging:
https://www.nia.nih.gov/alzheimers/early-onset-alzheimers-disease-resource-list

If family members are in the caregiver role, assess their well-being and coping strategies. Educate them about available support groups. Keep in mind that many support groups developed for Alzheimer disease are geared toward individuals over age 65. You may need to research support groups in your area for patients with early-onset Alzheimer disease.

Additionally, educate the family about how to deal with difficult behaviors, avoid triggers, administer medication safely, and monitor for adverse reactions. Stress the importance of maintaining a consistent routine. Caregivers need to be prepared for hallucinations, delusions, paranoia, resisting care, and, in the later stages, anger and potential physical abuse. Caring for a person with Alzheimer disease can be frustrating and exhausting because there's no end in sight and their loved one will continue to deteriorate. Another stressor for family members is that their loved one will eventually forget them and all memories associated with them. In many cases, these family caregivers will be responsible for their loved one 24 hours a day with no breaks. However, with proper education, you can increase the quality of life for both your patients and their caregivers.

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Keeping up to date

To provide appropriate care and education for your patients and their families, it's essential that you stay on top of current research in the area of early-onset Alzheimer disease. A variety of research studies are being conducted on early-onset Alzheimer disease and it's hoped that this research will shed light on changes that occur in the brain before and after the development of symptoms, leading to innovative treatments and disease prevention. ■

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