In-service Training

Alzheimer's Disease: An In-Depth Overview

Length: 1.5 hours

Goals: By the end of this training session, the participant will be able to:

- Describe the role of plaques and tangles in Alzheimer's disease.
- Name at least 5 symptoms of Alzheimer's disease.
- Identify at least two techniques used in diagnosing Alzheimer's disease.
- Identify at least two medical approaches to treating Alzheimer's disease.

Suggestions: This is an in-depth overview of Alzheimer's disease. Consider reviewing reference information prior to providing the in-service or arrange for a guest speaker from the Alzheimer's Association or other group.

Alzheimer's Disease

Adapted from the National Institutes of Health (NIH) Pamphlet: "Alzheimer's Disease, Unraveling the Mystery" which can be obtained at www.nih.gov.

What Is Alzheimer's Disease?

"With Alzheimer's people, there's no such thing as having a day which is like another day. Every day is separate...it's as if every day you have never seen anything before like what you're seeing right now." -- Cary Henderson

This excerpt from the journal of a man with Alzheimer's disease offers a glimpse of what it's like to be one of the 4,000,000 people in the United States who have this progressive, degenerative brain disorder. Cary Henderson, a history professor in Virginia, was diagnosed with Alzheimer's disease at age 55.

Alzheimer's disease is one of the most common causes of the loss of mental function known broadly as dementia. This type of dementia proceeds in stages, gradually destroying memory, reason, judgment, language, and eventually the ability to carry out even the simplest of tasks.

"You just feel that you are half a person," Henderson says in his narrative, which was dictated on a tape recorder in the early stages of the disease. "And you so often feel that you are stupid for not remembering things or for not knowing things... Just the knowledge that I've goofed again or I said something wrong or I feel like I did something wrong or that I didn't know what I was saying or I forgot--all of these things are just so doggone common..."

Such personal accounts inevitably make one ask, why? What causes this disease? Can't anything be done to stop it or to prevent it? Scientists ask essentially the same questions, and this booklet describes their search for answers. It provides a brief overview of dozens of paths that are bringing us closer to ways of managing, and eventually defeating, Alzheimer's disease.

Symptoms of Alzheimer's Disease

Alzheimer's is a progressive disease, the symptoms growing worse with time. Yet it is also a variable disease. Symptoms progress at different rates and in different patterns. Thus one patient may begin to have problems with muscular coordination earlier than another or retain some memories longer.

Researchers, who need to have some standard way to measure the progression of symptoms, have devised several different scales. One, the Clinical Dementia Rating (CDR), delineates five stages in the disease, while another, the Global Dementia Scale (GDS), has seven stages.

However most people who work with patients and families think of the disease in three phases: mild, moderate, and severe. These three stages can be viewed as follows, keeping in mind that the divisions are approximate, that they overlap, and that the appearance and progression of symptoms vary from one individual to the next.

Mild Symptoms

- Confusion and memory loss
- Disorientation; getting lost in familiar surroundings
- Problems with routine tasks
- Changes in personality and judgment

Moderate Symptoms

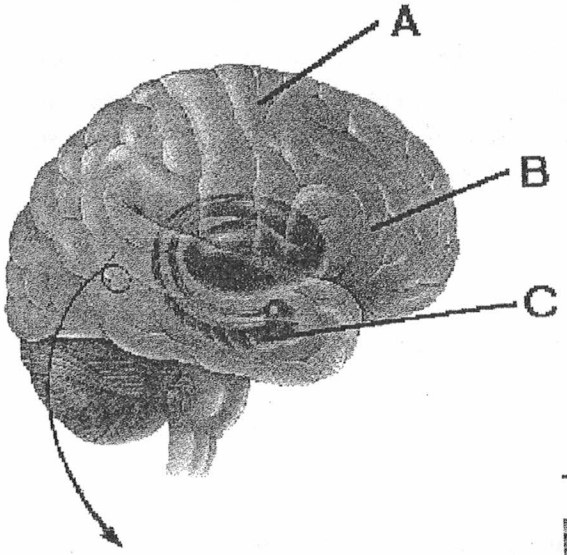
- Difficulty with activities of daily living, such as feeding and bathing
- Anxiety, suspiciousness, agitation
- Sleep disturbances
- Wandering, pacing
- Difficulty recognizing family and friends

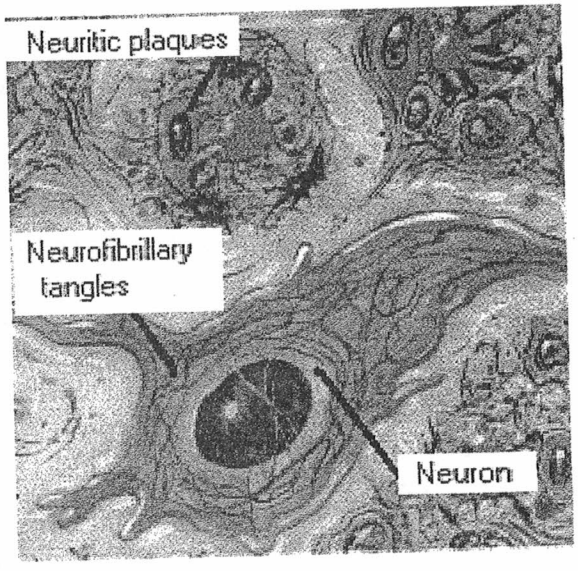
Severe Symptoms

- Loss of speech
- Loss of appetite; weight loss
- Loss of bladder and bowel control
- Total dependence on caregiver

The Brain and Alzheimer's Disease

The images below show the cerebral cortex **(A)**, involved in conscious thought and language; the basal forebrain **(B)**, which has large numbers of neurons containing acetylcholine, a chemical important in memory and learning; the hippocampus **(C)**, which is essential to memory storage; neuritic plaques; and neurofibrillary tangles. Alzheimer's disease attacks nerve cells (neurons) in several regions of the brain. The earliest signs of Alzheimer's are found in the nearby entorhinal cortex (not shown). Hallmarks of Alzheimer's disease include neuritic plaques (outside neurons), and neurofibrillary tangles (inside neurons).





Plaques and Tangles

A report like this one would not have been possible 20 years ago, when very little was known about Alzheimer's disease. But it is by no means a new disease. Ancient Greek and Roman writers described symptoms similar to those of Alzheimer's disease. In the 16th century, Shakespeare wrote about very old age as a time of "second childishness and mere oblivion," suggesting that the symptoms of Alzheimer's disease, or something quite similar, were known and recognized then.

These characteristic symptoms acquired a name in the early part of the 20th century when Alois Alzheimer, a German physician, described the signs of the disease in the brain. Alzheimer had a patient in her fifties who suffered from what seemed to be a mental illness. But when she died in 1906, an autopsy revealed dense deposits, now called plaques, outside and around the nerve cells in her brain. Inside the cells were twisted strands of fiber, or neurofibrillary tangles. Today, a definite diagnosis of Alzheimer's disease is still only possible when an autopsy reveals these hallmarks of the disease (plaques and tangles).

Plaques and tangles remained mysterious substances until the 1980's, when neuroscientists--the scientists who study the brain--discovered the proteins that make up these telltale anomalies. As research progresses, it is turning up clues to how plaques and tangles develop and how they relate to other changes in the brain.

In the meantime, much more about the disease has come to light. We now know that Alzheimer's begins in a part of the brain called the entorhinal cortex and proceeds to the hippocampus, a waystation important in memory formation. It then gradually spreads to other regions, particularly the cerebral cortex. This is the outer area of the brain, which is involved in functions such as language and reason. In the regions attacked by Alzheimer's, the nerve cells or neurons degenerate, losing their connections with other neurons. Some neurons die.

The Course of the Disease

As brain cells in the hippocampus neurons degenerate, short-term memory falters. Often the ability to perform routine tasks begins to deteriorate as well. Henderson describes the difficulty and frustration he feels when he tries to open a can of food for the family's dog. "...the best I could do was to try to dig a hole, make a little perforation and see if I could extend the side of it--and it was something like a panic...I'm too clumsy because of the Alzheimer's.... Right now, the doggie seems to be in fairly good shape. I'm not too sure I am."

As Alzheimer's disease spreads through the cerebral cortex, it begins to take away language. "Lately, I've had trouble with words (practically have to play charades)" says Letty Tennis, a North Carolina woman with Alzheimer's disease who also kept a journal. Tennis talks about how her judgment is changing and refers to the emotional outbursts that are common in this disease. "We had a great time shopping, but...I bought everything in sight...My poor dear husband didn't stop me very much unless it was too outrageous and then I'd get very angry. I bought a pair of boots--galoshes really...and I told George it's something I've always wanted so we bought them and when we got home I had no memory of buying them--they were awful and cost $40...I used to be the sensible one in the family."

Disturbing behaviors, such as wandering and agitation, beset many people as the disease progresses. In its final stages Alzheimer's disease wipes out the ability to recognize even close family members or to communicate in any way. All sense of self seems to vanish, and the individual becomes completely dependent on others for care.
Patients often live for years with this condition, dying eventually from pneumonia or other diseases. The duration of Alzheimer's disease from time of diagnosis to death can be 20 years or more. The average length is thought to be in the range of 4 to 8 years.

Diagnosing Alzheimer's Disease: Current Tools

A definite diagnosis of Alzheimer's disease is still only possible during autopsy when the hallmark plaques and tangles can be detected. But with the tools now available, physicians and patients can count on 85 to 90 percent accuracy, according to studies in which clinical diagnosis was later confirmed by autopsy. Clinicians diagnose "possible Alzheimer's disease" and "probable Alzheimer's disease" using criteria established in 1984 by the National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Diseases Association (NINCDS/ADRDA Guidelines).

Diagnostic Tools

- Patient history
  A detailed description of how and when symptoms developed; the patient's and family's medical history; and an assessment of the patient's emotional status and living environment.
- Physical examination and laboratory tests
  Standard medical tests to help identify other possible causes of dementia.
- Brain scans
  Usually a computed tomography (CT) scan or magnetic resonance imaging (MRI) to detect strokes or tumors that could be causing symptoms of dementia.
- Neuropsychological testing
  Usually several different tests in which patients answer questions or complete tasks that measure memory, language skills, ability to do arithmetic, and other abilities related to brain functioning.

Biological Markers

The tantalizing possibility that somewhere outside the brain there is a biological marker for Alzheimer's disease--an abnormal protein, for instance, that shows up in blood as well as the brain--continues to attract investigators.

Over the past decade, small preliminary studies have raised hope--and headlines--for several different markers. So far none has stood up under closer scrutiny. Still under consideration is a marker that may show up during a simple eye test, according to one study. In this study, a drug commonly used in eye examinations to enlarge the pupils, called tropicamide, increased the pupil size of suspected Alzheimer's disease patients in the study more than in other older people. This study involved fewer than 20 patients. Again, the next step is larger studies.

Imaging

Scans of the brain already help in diagnosing Alzheimer's disease by ruling out other forms of dementia, such as tumors and signs of stroke. But researchers also are using scans to search for markers of Alzheimer's disease itself.

Their tools include PET, which traces blood flow and metabolism in the brain and SPECT (*single photon emission computed tomography*) which also measures blood flow. Another imaging technique, magnetic *resonance imaging* (MRI), lets researchers view the brain's structure in cross section.

All of the imaging techniques--PET, SPECT, MRI, and MRSI--are still primarily research tools. However, they hold the promise of leading to an early and cost-effective method for diagnosing Alzheimer's disease.

Investigating Treatments

The rapid pace of research on Alzheimer's disease over the past 20 years has opened numerous pathways that could lead to effective treatments for the disease. Treatment research falls into two general categories. First, neuroscientists have turned up an array of substances in the brain that seem to be related to the disease and these are potential targets for biomedical treatments.
A second group of studies focuses on management of the disease. This area of research is looking for ways to treat the symptoms of Alzheimer's disease and slow its progress, either through drugs or behavioral approaches.

Potential Medical Treatments

Cholinergic replacement therapy
The discovery that the neurotransmitter acetylcholine declines in Alzheimer's disease led naturally to the hypothesis that replacing acetylcholine could stop the disease. Since that finding, many scientists have looked for compounds that can either increase the levels of acetylcholine, replace it, or slow its breakdown. This search has taken them into a broader territory that includes the cells that use acetylcholine and the enzymes and other proteins that take part in its manufacture or activity--a grouping known as the *cholinergic system*.

One member of the cholinergic system is acetylcholinesterase (often referred to simply as cholinesterase), the enzyme that breaks down acetylcholine after it crosses the synapse. Many of the experimental Alzheimer's drugs developed to date are cholinesterase inhibitors; that is, they are designed to suppress cholinesterase so that acetylcholine will not be broken down as quickly.

The discovery of acetylcholine deficits in Alzheimer's disease also raised hope that choline and lecithin, if added to the diet, could help in treating Alzheimer's disease. The body uses these nutrients to synthesize acetylcholine. Trials with the two substances have been disappointing so far, with choline supplements having no effect on cognitive function and lecithin only a slight effect in a few patients. Researchers are still interested in other substances that may enhance the availability of acetylcholine.

Estrogen replacement
Estrogen made front page headlines in late 1993 when scientists reported a possible link between it and Alzheimer's disease. In a study of thousands of women in a southern

California retirement community, those who had taken estrogen after menopause had lower rates of Alzheimer's disease than those who had not taken estrogen.

It was not the first time that neuroscientists had taken notice of this hormone. Earlier studies sought connections between estrogen and mental skills with mixed results. One study of 800 women found that taking estrogen after menopause had no effect on later mental functions. Another showed that estrogen did not seem to protect intellectual function in general, although it did enhance verbal memory.

Nonetheless, the California study and others have provided enough evidence in favor of estrogen to spur much larger population studies of postmenopausal estrogen therapy and its possible preventive effect on Alzheimer's. A clinical trial of estrogen as a treatment in early-stage Alzheimer's disease is under way.

In the meantime, biochemical studies have come up with a string of related findings. Researchers have found that the cholinergic neurons of the brain have numerous estrogen receptors, and they occur on the same neurons that have receptors for nerve growth factor; that estrogen in animals boosts levels of nerve growth factor; and that estrogen injected in rats' brains strongly affects neurons in the cerebral cortex and the hippocampus--regions affected by Alzheimer's disease. These pieces of evidence have given rise to the hypothesis that nerve growth factor and estrogen interact in some way to protect cholinergic neurons from degenerating.

It is much too early, of course, to tell whether taking estrogen does reduce the risk of Alzheimer's disease. Like the other areas of treatment research, this one is still at a preliminary stage. And since estrogen replacement therapy following menopause is not recommended for all women, scientists have urged caution in interpreting the findings to date.

Calcium regulators

The theory that a rise in calcium levels in neurons is the final step in the biochemical pathway leading to Alzheimer's disease has raised more treatment possibilities. A drug that could keep this final step from taking place might prevent or help slow down the disease.

Drugs called calcium channel blockers, already in wide use to treat high blood pressure and other problems, might fill this role, say some researchers. Calcium enters and exits neurons through several kinds of channels, so finding the right channel and channel

blocker may be a complex task. Currently one drug company is testing a channel blocker in Alzheimer's patients and other calcium regulators are being considered for trials.

Antioxidants

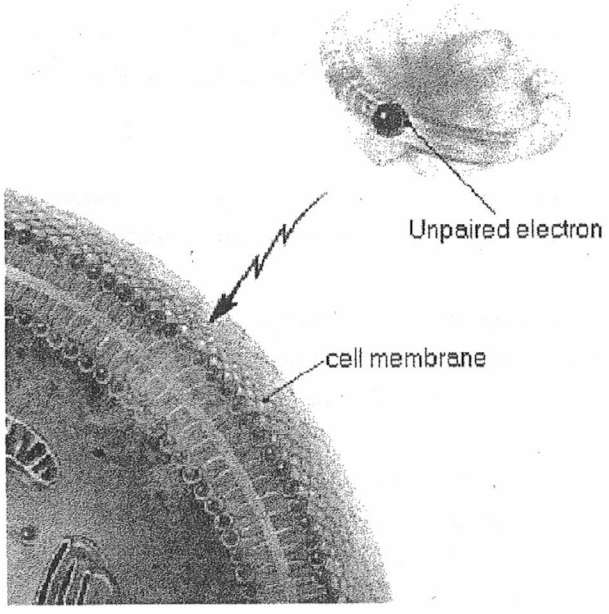
Still another theory about calcium imbalance points to out-of-control molecules known as *oxygen free radicals* and the agents that disarm them, including *antioxidants*.

A free radical is a molecule with an unpaired electron in its outer shell. Ordinarily an oxygen molecule, like other molecules, has an even number of electrons in orbit. But the normal process of turning food into energy--metabolism--produces oxygen radicals with an odd number of electrons. The oxygen radical is extremely reactive; it will latch readily onto another molecule--a part of the membrane or a unit of DNA, for instance. When this happens, it can set off a chain reaction, releasing chemicals that can be harmful to the cell. Scientists theorize that damage from oxygen radicals plays a role in aging as well as in diseases ranging from glaucoma to cancer.

In Alzheimer's disease, free radicals are suspects for several reasons. Some researchers hypothesize that free radicals upset the delicate membrane machinery that regulates what goes into and out of a cell, such as calcium. Free radicals may also have a connection with beta amyloid. One study has found that in neuritic plaques, beta amyloid breaks easily into fragments, releasing free radicals.

The body has certain lines of defense against oxygen free radicals. Enzymes like can disarm the damaging oxygen molecules, and the vitamins in food known as antioxidants--vitamins C and E and beta-carotene --also counter free radicals.

Several proposed treatments for Alzheimer's hinge on the theory that free-radical damage plays a key role in the disease and that antioxidants, therefore, should be able to slow down its progression.



Free Radicals: an unpaired electron approaching a nerve cell membrane. This kind of oxygen molecule can set off a chain reaction that can harm neurons, perhaps playing a role in Alzheimer's disease.

Anti-inflammatory drugs

Alzheimer's rates may be lower among people who take anti-inflammatory drugs than among those who do not. In a recent study of twins, one member of each pair had Alzheimer's and one did not. Many of the twins who did not have the disease had one thing in common: they took anti-inflammatory drugs for arthritis. A clinical trial is now testing whether the anti-inflammatory drug prednisone can slow the progress of the disease in its early stages.

Conclusion

What is obvious is that we have learned much about Alzheimer's disease, but even more research is necessary to provide better medical treatments. Use this information to better understand what is happening to the brains of residents you are caring for that are affected by Alzheimer's disease.

Quiz

ALZHEIMER'S DISEASE: AN IN-DEPTH OVERVIEW

True and False

1. T F Unlike other dementias, Alzheimer's disease does not go through obvious stages of progression.

2. T F Symptoms of Alzheimer's disease can be grouped as mild, moderate and severe.

3. T F Difficulty in performing activities of daily living does not typically occur until the final stages of Alzheimer's disease.

4. T F Alzheimer's disease cannot be definitively diagnosed until an autopsy is performed.

Multiple Choice

5. Which of the following are considered symptoms of Alzheimer's disease?
   a. Improved short-term memory
   b. Getting lost in familiar environments
   c. Increased production of acetylcholine
   d. Loss of vision

6. What role do neuritic plaques play in Alzheimer's disease?
   a. The help heal brains cells.
   b. They decrease the destructive proteins that cause Alzheimer's disease.
   c. They contribute to degeneration of brain cells.
   d. None of the above

7. How do new medications called cholinesterase inhibitors help to treat Alzheimer's?
   a. They lead to an increase in the essential neurotransmitter acetylcholine.
   b. They lead to an increase in the essential neurotransmitter serotonin.
   c. They are only experimental and have not been shown to work.
   d. They improve oxygen flow to the brain.

8. Which of the following is not a medical approach to treating Alzheimer's disease?
   a. Surgical removal of dead brain cells
   b. Estrogen replacement
   c. Increasing available acetylcholine
   d. Antioxidant therapy

Bibliography

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Orientation/In-Service Sign-in Sheet

Orientation/In-Service Topic/Title:	
Date:	Location:
Instructor/Title/Signature:	
Notes:	

Name (print)	Signature

Certificate of Completion

THIS IS TO CERTIFY THAT

HAS COMPLETED THE FOLLOWING IN-SERVICE TRAINING

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Administrator/Instructor

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Date