National Institute on Aging

National Institutes of Health

ALZHEIMER'S DISEASE

Unraveling the Mystery

The Impact of AD

Once considered a rare disorder, Alzheimer's disease is now seen as a major public health problem that is seriously affecting millions of older Americans and their families.

The Federal government's lead agency for Alzheimer's disease research is the National Institute on Aging, part of the National Institutes of Health. NIH is part of the U.S. Department of Health and Human Services.

Alzheimer's Disease: Unraveling the Mystery

- What is AD? (slides 4 – 6)
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What is AD?

Alzheimer's disease is an irreversible, progressive brain disease that slowly destroys memory and thinking skills.

Although the risk of developing AD increases with age – in most people with AD, symptoms first appear after age 60 – AD is not a part of normal aging. It is caused by a fatal disease that affects the brain.

What is AD?

AD Statistics….

- AD is the most common cause of dementia among people age 65 and older.
- Scientists estimate that around 4.5 million people now have AD.
- For every 5-year age group beyond 65, the percentage of people with AD doubles.

- By 2050, 13.2 million older Americans are expected to have AD if the current numbers hold and no preventive treatments become available.

What is AD?

Where are people with AD cared for?

- home
- assisted living facilities (those in the early stages)
- nursing homes (special care units)

- The national cost of caring for people with AD is about $100 billion every year.

Inside the Human Brain

- The Brain's Vital Statistics (slide 8)
- The Three Main Players (slides 9 – 11)
- Other Crucial Parts (slide 12)
- The Brain in Action (slide 13)
- Neurons (slide 14)

Inside the Human Brain

To understand Alzheimer's disease, it's important to know a bit about the brain…

The Brain's Vital Statistics

- Adult weight:
  about 3 pounds
- Adult size:
  a medium cauliflower
- Number of neurons:
  100,000,000,000
  (100 billion)
- Number of synapses
  (the gap between neurons):
  100,000,000,000,000
  (100 trillion)

Inside the Human Brain

The Three Main Players

1. Cerebral Hemispheres – where sensory information received from the outside world is processed; this part of the brain controls voluntary movement and regulates conscious thought and mental activity:
   - accounts for 85% of brain's weight
   - consists of two hemispheres connected by the corpus callosum
   - is covered by an outer layer called the cerebral cortex

Inside the Human Brain

The Three Main Players

2. Cerebellum – in charge of balance and coordination:
   - takes up about 10% of brain
   - consists of two hemispheres
   - receives information from eyes, ears, and muscles and joints about body's movements and position

Inside the Human Brain

The Three Main Players

3. Brain Stem – connects the spinal cord with the brain
   - relays and receives messages to and from muscles, skin, and other organs
   - controls automatic functions such as heart rate, blood pressure, and breathing

Inside the Human Brain

Other Crucial Parts

- Hippocampus: where short-term memories are converted to long-term memories
- Thalamus: receives sensory and limbic information and sends to cerebral cortex
- Hypothalamus: monitors certain activities and controls body's internal clock
- Limbic system: controls emotions and instinctive behavior (includes the hippocampus and parts of the cortex)

Inside the Human Brain

The Brain in Action

Hearing Words

Speaking Words

Seeing Words

Thinking about Words

Different mental activities take place in different parts of the brain. Positron emission tomography (PET) scans can measure this activity. Chemicals tagged with a tracer “light up” activated regions shown in red and yellow.

Inside the Human Brain

Neurons

- The brain has billions of neurons, each with an axon and many dendrites.
- To stay healthy, neurons must communicate with each other, carry out metabolism, and repair themselves.
- AD disrupts all three of these essential jobs.

AD and the Brain

- Plaques and Tangles (slides 16 – 18)
- The Changing Brain in AD (slides 19 – 22)

AD and the Brain

Plaques and Tangles: The Hallmarks of AD

The brains of people with AD have an abundance of two abnormal structures:

- beta-amyloid plaques, which are dense deposits of protein and cellular material that accumulate outside and around nerve cells
- neurofibrillary tangles, which are twisted fibers that build up inside the nerve cell

An actual AD plaque

An actual AD tangle

AD and the Brain

Beta-amyloid Plaques

Amyloid precursor protein (APP) is the precursor to amyloid plaque.

1. APP sticks through the neuron membrane.
2. Enzymes cut the APP into fragments of protein, including beta-amyloid.
3. Beta-amyloid fragments come together in clumps to form plaques.

In AD, many of these clumps form, disrupting the work of neurons. This affects the hippocampus and other areas of the cerebral cortex.

AD and the Brain

Neurofibrillary Tangles

Neurons have an internal support structure partly made up of microtubules. A protein called *tau* helps stabilize microtubules. In AD, *tau* changes, causing microtubules to collapse, and *tau* proteins clump together to form neurofibrillary tangles.

AD and the Brain

Pet Scan of
Normal Brain

The Changing Brain in Alzheimer's Disease

No one knows what causes AD to begin, but we do know a lot about what happens in the brain once AD takes hold.

Pet Scan of Alzheimer's
Disease Brain

AD and the Brain

Preclinical AD

- Signs of AD are first noticed in the entorhinal cortex, then proceed to the hippocampus.
- Affected regions begin to shrink as nerve cells die.
- Changes can begin 10-20 years before symptoms appear.
- Memory loss is the first sign of AD.

AD and the Brain

Mild to Moderate AD

- AD spreads through the brain. The cerebral cortex begins to shrink as more and more neurons stop working and die.
- *Mild AD signs* can include memory loss, confusion, trouble handling money, poor judgment, mood changes, and increased anxiety.
- *Moderate AD signs* can include increased memory loss and confusion, problems recognizing people, difficulty with language and thoughts, restlessness, agitation, wandering, and repetitive statements.

AD and the Brain

Severe AD

- In severe AD, extreme shrinkage occurs in the brain. Patients are completely dependent on others for care.
- Symptoms can include weight loss, seizures, skin infections, groaning, moaning, or grunting, increased sleeping, loss of bladder and bowel control.
- Death usually occurs from aspiration pneumonia or other infections. Caregivers can turn to a hospice for help and palliative care.

AD Research: Finding New Answers and Asking Better Questions

- The Search for Causes (slides 24 – 28)
- Diagnosing AD (slides 29 – 30)
- Clinical Trials (slide 31)
- The Search for Treatments (slides 32-33)
- New NIA Study (slide 34)
- Managing the Symptoms of AD (slide 35)

AD Research: the Search for Causes

- AD develops when genetic, lifestyle, and environmental factors work together to cause the disease process to start.
- In recent years, scientists have discovered genetic links to AD. They are also investigating other factors that may play a role in causing AD. NIA-funded Alzheimer's Disease Centers (ADCs) across the country are leading the research efforts looking into causes, diagnosis, and treatment of AD.

AD Research: the Search for Causes

Genetic Studies

The two main types of AD are early-onset and late-onset:

- Early-onset AD is rare, usually affecting people aged 30 to 60 and usually running in families. Researchers have identified mutations in three genes that cause early-onset AD.
- Late-onset AD is more common. It usually affects people over age 65. Researchers have identified a gene that produces a protein called apolipoprotein E (ApoE). Scientists believe this protein is involved in the formation of beta-amyloid plaques.

AD Research: the Search for Causes

Late-onset AD Genetics Study

- Partnership between the NIA and the Alzheimer's Association
- Need to recruit a total of 1,000 families to find the remaining late-onset risk factor genes
- 2 or more living siblings with AD
- One other living family member with or without AD
- Contact: e-mail: alzstudy@iupui.edu or Website: www.ncrad.org

AD Research: the Search for Causes

Studies at the Cellular and Molecular Level

- Oxidative damage from free radical molecules can injure neurons.

- Homocysteine, an amino acid, is a risk factor for heart disease. A study shows that an elevated level of homocysteine is associated with increased risk of AD.
- Scientists are also looking at inflammation in certain regions of the brain and strokes as risk factors for AD.

AD Research: the Search for Causes

Epidemiologic Studies

Scientists examine characteristics, lifestyles, and disease rates of groups of people to gather clues about possible causes of AD. The NIA is currently funding epidemiologic studies in a variety of different groups. Two of the studies focus on religious communities. Researchers conduct yearly exams of physical and mental status, and studies of donated brains at autopsy. Some early results indicate:

- Mentally stimulating activity protects the brain in some ways.
- In early life, higher skills in grammar and density of ideas are associated with protection against AD in late life.

AD Research: Diagnosing AD

Experienced physicians in specialized AD centers can now diagnose AD with up to 90 percent accuracy. Early diagnosis has advantages:

- Doctors can rule out other conditions that may cause dementia.
- If it is AD, families have more time to plan for the future.
- Treatments can start earlier, when they may be more effective.
- It helps scientists learn more about the causes and development of AD.

AD Research: Diagnosing AD

Physicians today use a number of tools to diagnose AD:

- a detailed patient history
- information from family and friends
- physical and neurological exams and lab tests
- neuropsychological tests
- imaging tools such as CT scan, or magnetic resonance imaging (MRI). PET scans are used primarily for research purposes

AD Research: Clinical Trials

Clinical trials are the primary way that researchers find out if a promising treatment is safe and effective.

- Trials examine approved drugs to see if they can be used for other purposes, or look at experimental drugs.
- Participating in a trial means regular contact with the study team, who can provide state-of-the-art AD care.

AD Research: the Search for Treatments

Drugs used to treat mild to moderate AD symptoms include:

- Aricept
- Exelon
- Reminyl

An additional drug, Namenda, has been approved to treat symptoms of moderate to severe AD. These drugs can help improve some patients' abilities to carry out activities up to a year or so, but they do not stop or reverse AD.

Scientists are also studying agents that someday may be useful in preventing AD. For example, they have experimented with a vaccine against AD. Although the first clinical trial was stopped due to side effects in some participants, valuable information was gathered.

AD Research: the Search for New Treatments

Researchers also are looking at other treatments, including:

- cholesterol-lowering drugs called statins
- anti-oxidants (vitamins) and folic acid
- anti-inflammatory drugs
- substances that prevent formation of beta-amyloid plaques
- nerve growth factor to keep neurons healthy

AD Research: New NIA Study

The NIA is launching a new research partnership, called the Neuroimaging and Biomarkers of AD Initiative, to study how the brain changes in Mild Cognitive Impairment (MCI) and AD.

- Using MRIs and PET scans conducted at regular intervals, researchers hope to learn precisely when and where in the brain problems occur.
- Researchers will also examine blood samples to check for higher levels of abnormal substances that could be considered “biomarkers” of AD.

AD Research: Managing Symptoms

Between 70 to 90% of people with AD eventually develop behavioral symptoms, including sleeplessness, wandering and pacing, aggression, agitation, anger, depression, and hallucinations and delusions. Experts suggest these general coping strategies for managing difficult behaviors:

- Stay calm and be understanding.
- Be patient and flexible. Don’t argue or try to convince.
- Acknowledge requests and respond to them.
- Try not to take behaviors personally. Remember: it’s the disease talking, not your loved one.

Experts encourage caregivers to try non-medical coping strategies first. However, medical treatment is often available if the behavior has become too difficult to handle. Researchers continue to look at both non-medical and medical ways to help caregivers.

Improving Support for Families and Other Caregivers

- Who are the AD Caregivers? (slide 37)
- Demands of Caregiving (slide 38)
- Technology and Caregiving (slide 39)
- National Support for Caregivers (slide 40)
- How to Contact the ADEAR Center (slide 41)

Support for Caregivers

Who are the AD Caregivers?

- Spouses – the largest group. Most are older with their own health problems.
- Daughters – the second largest group. Called the "sandwich generation," many are married and raising children of their own. Children may need extra support if a parent's attention is focused on caregiving.
- Grandchildren – may become major helpers.

- Daughters-in-law – the third largest group.
- Sons – often focus on the financial, legal, and business aspects of caregiving.
- Brothers and Sisters – many are older with their own health problems.
- Other – friends, neighbors, members of the faith community.

Support for Caregivers

Demands of Caregiving

AD takes a huge physical and emotional toll. Caregivers must deal with changes in a loved one's personality and provide constant attention for years. Thus, caregivers are especially vulnerable to physical and emotional stress.

- Peer support programs can help link caregivers with trained volunteers. Other support programs can offer services geared to caregivers dealing with different stages of AD.

Support for Caregivers

Technology and Caregiving

The NIA is studying how computers can provide information and support to family caregivers through:

- computer-based bulletin boards
- chat rooms
- Q & A modules
- medical advice forums

These features have become very popular among users because they reach many people at once, are private and convenient, and are available around the clock.

National Support for Caregivers

Alzheimer's Association

- Local chapters provide referrals to area resources and services, and sponsor the Safe Return Program, support groups, and educational programs:

1-800-272-3900

www.alz.org

Eldercare Locator

- Nationwide service of the Federal Government helps caregivers locate local support and resources:

1-800-677-1116

www.eldercare.gov

For more information on Alzheimer's disease and a list of the NIA-funded Alzheimer's Disease Centers, contact the Alzheimer's Disease Education and Referral (ADEAR) Center at:

1-800-438-4380

www.alzheimers.org

The ADEAR Center is a service of:

- National Institute on Aging, part of the

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This PowerPoint slideshow is based on the publication *Alzheimer's Disease: Unraveling the Mystery.* Contact the ADEAR Center for free copies.