When you touch a hot stove, you know you will burn your finger. In this situation, cause and effect are clear. With Alzheimer’s disease, however, the cause and effect relationship is both complex and elusive. Research indicates that genetic, environmental, and lifestyle factors work together in some way to trigger the disease and cause it to progress, but the impact of these individual factors differs for each person affected.

Alzheimer’s disease is named after Alois Alzheimer, who discovered abnormal protein plaques and tangles in the brain of a woman who died of dementia. These plaques and tangles are now considered the hallmarks of AD, but in recent years, researchers have found that they also appear in the brains of many people who don’t show signs of the disease.

One well-known and ongoing study of Alzheimer’s disease is the Rush Memory and Aging Project. It involves 1200 elderly volunteers who are evaluated yearly and have agreed to donate their brains after death. To date, of the 141 participants who have died, 80 had “sufficient Alzheimer’s disease pathology” (plaques and tangles) in their brains to have been reasonably expected to show signs of Alzheimer’s disease in life. Yet only 47 of them had been diagnosed with probable AD! Why didn’t the other 33 exhibit signs of dementia?

Obviously, their brains were protected in some way, but exactly how remains a mystery.

The two most common risk factors for Alzheimer’s disease are age and genetics, neither of which we can control, but they are only a part of the story. Millions of people grow old without developing dementia. As for genetics, a rare form of Alzheimer’s disease called early-onset AD, which occurs in people between the ages of 30 and 65, is related to mutations on three chromosomes. Late-onset AD, which is much more common, develops after the age of 65, and the highest genetic risk factor found to date is the presence of the gene apolipoprotein E4 (APOE4); however, even this gene appears in only about 40% of people with AD according to the National Institute on Aging (NIA). Obviously, other factors are at work.

CONTINUED ON PAGE 2
The Rush Project also found that people who had multiple chronic diseases, such as AD and evidence of artery blockage were more likely to develop dementia. For this reason, the factors that contribute to heart disease are being studied for their possible link to Alzheimer's disease. Studies show that people who have high blood pressure and high cholesterol levels are at higher risk for heart attacks and other heart conditions, but can lowering blood pressure and cholesterol also play a role in lowering the risk for Alzheimer's disease?

Relationships between AD and other diseases are also being studied. People with diabetes are at higher risk for vascular dementia (dementia caused by strokes), and studies show a similar association between type 2 diabetes and AD. Researchers are particularly interested in the possible role of insulin resistance, which occurs when the body produces insulin, but cells don't use it properly. Too much insulin in the blood "may encourage inflammation and oxidative stress, both of which contribute to the damage seen in AD," according to the NIA (See Resources). This explains why Alzheimer's research is being done with anti-inflammatory drugs and anti-oxidant vitamins (particularly C and E).

Although our knowledge about the causes of AD is limited, we do know that maintaining a healthy lifestyle - eating right, exercising regularly - can help stave off a multitude of diseases!

Brain imaging is one new development in AD research, offering a possible way to identify damage to parts of the brain involved in memory before symptoms of the disease occur. Research suggests that the propensity to develop Alzheimer's disease begins long before old age. In one NIA-funded study comparing healthy older people and people diagnosed with possible or probable AD, scientists found that the healthy group had engaged in more mentally stimulating activities and spent more hours doing them during their early and middle adulthood than did those who ultimately developed AD. Most stimulating activities were relatively simple: reading newspapers, listening to the radio, playing puzzle games, or going to museums. This research offers yet another reason to pursue lifelong learning! .

**Key Points:**
- Brain imaging may help to reveal signs of changes in the brain before symptoms of AD are evident in a person's actions.
- Some studies indicate that people who begin healthy habits relatively early in life, such as keeping their brains positively stimulated, will have less likelihood of developing AD later in life.

The Long Road to Cause, Cure, and Prevention

*FROM PAGE ONE*
Interestingly, knowing the cause of a disease is not required in order to develop treatments for it. Millions of people benefit from treatments available for incurable conditions such as diabetes, Parkinson's disease, and arthritis. The same is true for Alzheimer's disease. No current medications can stop the progression of Alzheimer's disease, but the U.S. Food and Drug Administration (FDA) has approved five drugs to treat its cognitive symptoms.

Four of them are cholinesterase (KOH-luh-NES-ter-ays) inhibitors, which seem to prevent the breakdown of acetylcholine (a-SEA-til-KOH-lean). Acetylcholine is a chemical messenger that helps connect the brain's nerve cells and is important for learning and memory.

Cholinesterase inhibitors are prescribed for the treatment of mild to moderate AD to help delay symptoms or prevent them from becoming worse for a limited time. As AD progresses, the brain produces less and less acetylcholine; therefore, cholinesterase inhibitors eventually seem to lose their effect. Some people benefit more dramatically than others and for a longer period.

The fifth drug currently approved by the FDA works by regulating the activity of glutamate, a different chemical messenger involved in learning and memory. It was approved in 2003 for treatment of moderate to severe Alzheimer's disease and has benefits similar to the other four drugs.

Additionally, adverse reactions are not routinely monitored, and some supplements have known side effects that are potentially harmful. Ginkgo Biloba, for example, is known to reduce the ability of blood to clot, which could cause internal bleeding. It should not be taken in combination with other blood-thinning drugs, such as aspirin or warfarin.

Many more drugs are now in various phases of clinical trials, and current drugs are becoming available in more user-friendly forms.

While these drugs are imperfect, and in some people have side effects that limit the dosage a person can tolerate, they have been of great benefit to many. Caregivers of those on these medications tend to appreciate the extension of time that a person with AD can manage self-care issues such as dressing and using the bathroom. People with AD tend to appreciate the increased clarity they feel as a result of the medication.

Many people also use dietary supplements in an attempt to prevent dementia or delay its effects. While some of these, such as Ginkgo Biloba and Omega-3 fatty acids, show promise and are currently being studied, the FDA does not require rigorous scientific research for dietary supplements, which means they should always be used only under a doctor's supervision. Their purity, safety, and effectiveness are not well-regulated, so the composition of one brand may be quite different from another.

Ginkgo Biloba, for example, is known to reduce the ability of blood to clot, which could cause internal bleeding. It should not be taken in combination with other blood-thinning drugs, such as aspirin or warfarin.

RESOURCES

The material used as background for this issue came entirely from the website for the Alzheimer's Disease and Education Resource Center (ADEAR) which can be found at http://www.alzheimers.nia.nih.gov. Look under publications, and then under the headings "causes," "diagnosis," and "treatments." Information also came from the June 13, 2007 article "Study Finds Mix of Disease Processes at Work in Brains of Most people with Dementia" at that website.

The mailing address for the ADEAR Center is PO Box 8250, Silver Spring, MD 20907-8250, and the toll-free phone is 1-800-438-4380. Single copies of most ADEAR publications are free, and many are downloadable as pdf files.
The coach of the college baseball team, Bart Smart, was checking the grounds around the dormitory to make sure his boys were in by curfew. Suddenly he heard a loud crash and caught a glimpse of a man running into the dorm. Bart thought it was his star right-handed pitcher, Don Juan, but couldn’t see him clearly. By the time he crossed the grounds and entered Don’s room, Don was standing in the middle of the room with his right leg in his pants and his left leg out. He said, "I heard a loud crash and was just getting dressed to see what happened." Coach Smart, said, "Hardly. You just ran in here. You're grounded."

How could the coach be certain?

Let’s talk

Give participants a chance to express their ideas: How did Coach Smart know Don Juan was guilty? Don't judge the answers, but call attention to the process. What are the clues? What do they mean? What else needs to be known?

The purpose of this exercise is to gain insight into the complications of solving a mystery - or finding the cause of a serious disease. We not only need to know the facts that were presented in the story, but we have to understand the meaning of those facts: Bart knew Don was lying, that in fact he was getting undressed, not dressed as he claimed. How? Because, unless his leg is injured, a right-handed person will almost always put his left leg in his pants first when dressing.

Solving this puzzle requires knowing that key piece of trivia. Some people will find it interesting as they think about their own habits, but others will cry, "Foul!" because who really pays attention to such trivial details? That's precisely the point.

Solving a mystery often involves having specialized knowledge, without which, we will often make the wrong connections and run into dead-ends or be led on wild goose chases. Still, acquiring the key piece of knowledge often requires lots of experimentation and observation - lots of dead-ends and wild goose chases. In terms of finding the cause of Alzheimer's disease, we are still apparently missing some of both the pertinent connections and the meanings behind them.

Answer Key for Quiz on Page 5

1) b  2) d  3) b  4) d  5) c
Please answer the following questions based on the information on the previous pages.

1) The two most common risk factors for Alzheimer’s disease are increasing age and certain genetic factors. Not everyone who gets old will develop AD, but everyone with those genetic risk factors will.
   a. True
   b. False

2) Current research on the cause or causes of Alzheimer’s disease involves studying various other diseases, including:
   a. Diabetes
   b. Heart disease
   c. Arthritis and other inflammatory diseases
   d. All of the above
   e. A and B only

3) Currently, five drugs have been approved by the Food and Drug Administration for the treatment of Alzheimer’s disease. Only two of them actually stop the progression of the disease.
   a. True
   b. False

4) People who take dietary supplements such as Ginkgo Biloba or Omega-3 Fatty Acids should do so only under the supervision of their physicians because:
   a. Dietary supplements are not well-regulated for safety and effectiveness
   b. Composition varies among different brands
   c. Side effects and interactions with other drugs can be harmful
   d. All of the above
   e. A and C only

5) Not all treatments for Alzheimer’s disease are related to taking medicine. While all of the following are helpful, which of the following is likely to be LEAST beneficial in preventing or delaying AD?
   a. Pleasant social interaction with family and friends
   b. Eating a healthy diet
   c. Beginning an improved lifestyle after retirement when you have time to devote to it
   d. Getting regular exercise
   e. Keeping your brain active with mentally stimulating activities