Does statin use decrease the amount of Alzheimer disease pathology in the brain?

In this issue of Neurology®, Li and coauthors report the results of a study that looked at differences in the number of plaques and tangles in the brain at death between those who used statins (see below) and those who did not. Patients with Alzheimer disease (AD) develop clusters of protein in between the brain cells, called amyloid plaques, and groups of fibers inside of brain cells, called neurofibrillary tangles (figure).

WHAT ARE STATINS? Statins are a type of medication commonly used to treat high cholesterol. They have been shown to lower the risk of heart attack and stroke in people with a history of heart disease.2 Besides lowering cholesterol levels, statins may also help to lower the amount of swelling, free radicals, and small artery disease in the brain. Some researchers have seen that the number of people who get AD is lower among those taking statins than those not taking statins. Recent research has not shown that statin use prevents the development of AD.

WHAT WAS THE STUDY ABOUT? All the patients in this study were followed in the Adult Changes in Thought (ACT) study with regular screening tests for dementia. Although none of the subjects had problems with their thinking when they entered the study, some developed dementia before they died. When the authors began this study, 608 people taking part in the ACT study had died. The rate of death was lower in statin users than in nonusers. Of the 608 subjects who died, 110 of those had agreed to an examination of their brain at the time of their death. These 110 subjects tended to be older at death, and were more likely to be female and white than those who did not wish to participate. Thirty-six of the 110 subjects had been treated with a statin at some time in their life, and 74 had not. An equal percentage of subjects in each group developed dementia before death.

WHAT DID THE AUTHORS LOOK FOR? The amount of plaques and distribution of tangles in the brain were compared between those who had taken statins and those who had not. The authors also considered other things that might influence the amount of plaques and tangles, such as age at death, gender, level of thinking ability at the beginning of the study, brain weight, and the presence of small strokes.

WHAT ARE THE MAIN FINDINGS OF THIS STUDY? The main finding is that statin users were less likely to have a high degree of tangles in their brain at death than nonusers. The amount of plaques was not different between the two groups. Statin users were less likely to have the degree of both plaques and tangles typically seen in AD than the nonusers. However, the authors also report that because of differences in characteristics between those who agreed to brain examination at death and those who did not, and because of differences in the rate of death between statin users and nonusers, it is difficult to apply these results to the general, living population.

WHY IS THIS STUDY IMPORTANT? AD affects approximately 4.9 million people age 65 and older in the United States, with the number expected to rise to 7.7 million by 2030.3 Besides causing suffering to those affected and their caregivers, AD creates a high financial burden to family members and society. Right now there is no cure for AD. Drugs used...
to treat AD help with symptoms of the disease, but do not help the underlying causes. Studies looking at the effects of medicine on what is actually happening in the brain tissue are rare, and are extremely valuable, as we search for treatments to slow down or reverse the disease process.

**WHAT IS THE BOTTOM LINE?** This study shows that people who use a statin drug at some point in their life may have fewer brain tangles, a hallmark of AD, at death. Although the results of this study are promising, it has not yet been shown that statin use directly decreases AD pathology or delays the clinical manifestation of the disease in living people.

**REFERENCES**
About Alzheimer disease

WHAT IS AD? Alzheimer disease (AD) is a progressive illness in which patients have dementia, which means having memory loss and problems thinking that are bad enough to interfere with day-to-day functioning. Patients with AD develop clusters of protein in between the brain cells, called amyloid plaques, and groups of fibers inside of brain cells, called neurofibrillary tangles. About 24 million people have dementia in the world, with the number expected to rise to 81 million by 2040. AD is the most common cause of dementia, and accounts for 50 to 60% of all cases.

WHAT IS THE RELATIONSHIP BETWEEN CHOLESTEROL AND AD? At this time, no one knows for sure what role cholesterol plays in AD. All of us need some cholesterol in our diet in order to keep the cells in our body healthy. However, it has been shown by some researchers that animals given a high cholesterol diet develop greater than normal levels of a protein called $\beta$-amyloid ($\beta$-Amyloid). In AD, $\beta$-Amyloid builds up in the brain to form amyloid plaques. Animals given a drug to lower their cholesterol level had a decrease in the amount of these plaques. In humans with high cholesterol, some studies have shown an increased risk of getting AD, while other studies have shown a decreased risk of getting AD.4

The following portion of the ABOUT page is adapted from Jankowiak J. Depression may be another risk for Alzheimer’s dementia: your doctor can help. Neurology 2002;59:E4–E5.

WHAT ARE THE SYMPTOMS? Loss of recent memories is usually the earliest warning. For instance, the person will repeat stories in the same conversation. Other features include:

- Misplacing belongings
- Difficulty doing familiar tasks
- Increasing confusion and disorientation to time and place
- Trouble finding words, not following conversations
- Changes in mood or behavior
- Changes in personality

- Poor or decreased judgment
- Loss of initiative

KNOW THE WARNING SIGNS Unfortunately, in early stages, many people fail to recognize that something is wrong. They may assume that such behavior is a normal part of getting older. It is not. Symptoms may develop gradually and go unnoticed for a long time. Sometimes families do not act even when they suspect something is wrong. The key is early diagnosis. It is critical to see a doctor when you recognize or suspect AD symptoms.

HOW IS AD DIAGNOSED? When AD is suspected, it is important to have a complete medical and neurologic workup. The purpose of this evaluation is to uncover other causes of dementia that must be treated in very specific ways. This may include:

- A complete health history and physical examination
- Screening for depression
- Neurologic and mental status testing
- Blood and urine tests
- CT scan or MRI

WHAT CAUSES AD? The cause of AD is not fully known. It is not contagious. Aging and inherited or genetic factors seem to play an important role. The most common form of AD does not run in families.

WHAT ARE THE TREATMENTS? Although there is currently no cure for AD, there are treatments that may help.

Treat memory symptoms. The cognitive symptoms of AD should be treated as early as possible to slow the progression of the disease. Drugs called cholinesterase inhibitors may be considered in patients with mild to moderate disease. Vitamin E may also slow the progression, but should only be used if prescribed by the doctor.

Treat behavioral problems. Suspiciousness, aggression, or resistance to care may be treated first by understanding what triggers these behaviors.
Caregivers may learn how to change things in the environment to improve cooperation. Some examples include providing low lighting and music to improve eating behaviors, taking regular walks, scheduling toileting, and following consistent routines. Certain medications may also help, including drugs to treat depression.

**Caregivers need caring too.** Caregiver training programs to learn more about the disease and how to manage it help delay the time to nursing home placement. Support systems (adult day care, computer support networks, telephone support programs, and other respite programs) may also help.

**PREVENTION** Although there is no known way to prevent AD, researchers believe there are several things that will help keep your brain healthy:

- Avoid harmful substances—excessive drinking and drug abuse are thought to damage brain cells.
- Challenge yourself—read frequently, do crossword puzzles. Keep mentally active.
- Learn new skills. This strengthens the brain connections and promotes new ones.
- Exercise regularly—even low–moderate level activity such as walking or gardening three to five times per week can make you feel better.
- Stay socially active—family, friends, church, and a sense of community may all contribute to better brain health.

**CAREGIVER HEALTH** Families and friends can help by recognizing that AD impacts not only the patient, but also the primary caregiver. To take the best care of the patient with AD, the primary caregiver must take care of himself or herself. He or she should be encouraged to learn more about the disease, avoid isolation, and seek support from family, friends, and professionals.

**FOR MORE INFORMATION**
Alzheimer’s Association
www.alz.org
American Geriatrics Society
www.americangeriatrics.org
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