About statins and Alzheimer's disease

This fact sheet is prepared by the Alzheimer's Association for your information only and does not represent an endorsement of statins.

What are statins?

Statins is the common name for a class of drugs formally known as 3-hydroxy-3-methylglutaryl coenzyme A (HMG CoA) reductase inhibitors. These drugs lower levels of low-density lipoprotein (LDL) cholesterol—the type most strongly linked with coronary artery disease and stroke—by blocking a liver enzyme essential for cholesterol production. The U.S. Food and Drug Administration (FDA) approved the first statin in 1987. Statins now marketed in the United States include atorvastatin (Lipitor®), fluvastatin (Lescol®), lovastatin (Mevacor®), pravastatin (Pravachol®), simvastatin (Zocor®) and a number of other formulations.

Why are statins of interest in Alzheimer's disease?

Epidemiological studies have found a link between taking statins to reduce cholesterol levels and a decreased occurrence of Alzheimer's disease. Researchers explored the possibility of such a relationship because several previous studies suggested that people with cardiovascular risk factors have an increased Alzheimer risk. Other studies have shown that in the brain, the cholesterol-carrying protein apolipoprotein E (ApoE) promotes aggregation of the protein fragment beta-amyloid into the amyloid plaques that are a hallmark Alzheimer pathology. Further, individuals who have APOE-ε4—one of the three common variations of the gene that codes production of ApoE—have an increased likelihood of developing the common, late-onset form of Alzheimer's. These lines of evidence suggest that cholesterol levels and differences in the body's cholesterol-processing pathways may influence Alzheimer risk.

A small study involving 44 participants with normal cholesterol levels and a diagnosis of Alzheimer's has also found preliminary evidence that simvastatin may be of some benefit to individuals with Alzheimer's disease.

Gathering stronger evidence about the effectiveness of statins as a prevention or a treatment will require large-scale clinical trials comparing the occurrence of Alzheimer's in a group of participants randomly assigned to take statins to its frequency in a group similar in all important respects except not taking statins. The trials will need to include participants with normal cholesterol levels, because the effects of statins in this group have not been adequately studied. Additional work is also needed to determine the molecular mechanisms by which statins may modify pathological processes in Alzheimer's.

The Alzheimer's Association and most scientific experts believe that no one should take statins specifically to lower their risk of Alzheimer's until further research clarifies the possible relationship between statins and dementia. However, most physicians do advocate keeping one's cholesterol within levels recommended by the National Cholesterol Education Program of the National Heart, Lung, and Blood Institute, a division of the U.S. National Institutes of Health. The latest guidelines are summarized in: "Executive Summary of the Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III)," published in the May 16, 2001 issue of the *Journal of the American Medical Association* on pages 2486 – 2497. The guidelines are also posted on the Web site of the National Heart, Lung, and Blood Institute at: http://www.nhlbi.nih.gov/guidelines/cholesterol/index.htm.

Where can I get more information?

The Alzheimer's Association will update this fact sheet as scientists learn more about statins and Alzheimer's disease. For information about clinical trials of statins or answers to your other questions about Alzheimer's disease, please call

our 24/7 Nationwide Contact Center Helpline at 1.800.272.3900 or visit our Web site at www.alz.org.

You can find the preliminary studies mentioned in this fact sheet in these sources:

- Haley, Robert W. "Is There a Connection Between the Concentration of Cholesterol Circulating in Plasma and the Rate of Neuritic Plaque Formation in Alzheimer Disease?" (Editorial). *Archives of Neurology*, October 2000; 1410–1412.
- Jick, H., et al. "Statins and the Risk of Dementia." *The Lancet*, November 11, 2000; 1627–1631.
- Simons, M.; Schwartzler, F.; Lutjohann, D.; von Bergmann, K.; Beyreuther, K.; Dichgans, J.; Wormstall, H.; Hartmann, T.; Schultz, J.B. "Treatment with Simvastatin in Normocholesterolemic Patients with Alzheimer's Disease: A 26-Week, Randomized, Placebo-Controlled, Double-Blind Trial." *Annals of Neurology* September 2002; 52 (3): 346 – 350.
- Wolozin, Benjamin, et al. "Decreased Prevalence of Alzheimer Disease Associated with 3-Hydroxy-3-Methyglutaryl Coenzyme A Reductase Inhibitors." *Archives of Neurology*, October 2000;1439–1443.
- Yaffe, Kristine, et al. "Serum Lipoprotein Levels, Statin Use, and Cognitive Function in Older Women." *Archives of Neurology*, March 2002; 378–382.

Additional information about heart health and managing your cholesterol is available on the Web site of the American Heart Association at www.americanheart.org.

The Alzheimer's Association is fighting on your behalf to give everyone a reason to hope. For more information about Alzheimer research, treatment and care, please contact the Alzheimer's Association.

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Fact sheet updated **February 10, 2003**