

Alzheimers Disease



Ten Warning Signs of Alzheimer's Disease

Some change in memory is normal as we grow older, but the symptoms of Alzheimer's disease are more than simple lapses in memory. People with Alzheimer's experience difficulties communicating, learning, thinking, and reasoning — problems severe enough to have an impact on an individual's work, social activities, and family life.

The Alzheimer's Association believes that it is critical for people with dementia and their families to receive information, care, and support as early as possible. To help family members and health care professionals recognize warning signs of Alzheimer's disease, the Association has developed a checklist of common symptoms.

1. Memory loss. One of the most common early signs of dementia is forgetting recently learned information. While it's normal to forget appointments, names, or telephone numbers, those with dementia will forget such things more often and not remember them later.

2. Difficulty performing familiar tasks. People with dementia often find it hard to complete everyday tasks that are so familiar we usually do not think about how to do them. A person with Alzheimer's may not know the steps for preparing a meal, using a household appliance, or participating in a lifelong hobby.

3. Problems with language. Everyone has trouble finding the right word sometimes, but a person with Alzheimer's disease often forgets simple words or substitutes unusual words, making his or her speech or writing hard to understand. If a person with Alzheimer's is unable to find his or her toothbrush, for example, the individual may ask for "that thing for my mouth."

4. Disorientation to time and place. It's normal to forget the day of the week or where you're going. But people with Alzheimer's disease can become lost on their own street, forget where they are and how they got there, and not know how to get back home.

5. Poor or decreased judgment. No one has perfect judgment all of the time. Those with Alzheimer's may dress without regard to the weather, wearing several shirts or blouses on a warm day or very little clothing in cold weather. Individuals with dementia often show poor judgment about money, giving away large amounts of money to telemarketers or paying for home repairs or products they don't need.

6. Problems with abstract thinking. Balancing a checkbook may be hard when the task is more complicated than usual. Someone with Alzheimer's disease could forget completely what the numbers are and what needs to be done with them.

7. Misplacing things. Anyone can temporarily misplace a wallet or key. A person with Alzheimer's disease may put things in unusual places: an iron in the freezer or a wristwatch in the sugar bowl.

8. Changes in mood or behavior. Everyone can become sad or moody from time to time. Someone with Alzheimer's disease can show rapid mood swings—from calm to tears to anger—for no apparent reason.

9. Changes in personality. People's personalities ordinarily change somewhat with age. But a person with Alzheimer's disease can change a lot, becoming extremely confused, suspicious, fearful, or dependent on a family member.

10. Loss of initiative. It's normal to tire of housework, business activities, or social obligations at times. The person with Alzheimer's disease may become very passive, sitting in front of the television for hours, sleeping more than usual, or not wanting to do usual activities.

If you recognize any warning signs in yourself or a loved one, the Alzheimer's Association recommends consulting a physician. Early diagnosis of Alzheimer's disease or other disorders causing dementia is an important step in getting appropriate treatment, care, and support services.

Health Sciences Institute e-Alert

September 29, 2003

Dear Member,

President Ronald Regan is perhaps the world's most well known Alzheimer's disease patient. Here's a man, famous for his vigor and vitality during those years well beyond what we think of as "retirement" age. And yet, sadly, over the past decade, he's virtually disappeared from public life.

During that decade, the number of Alzheimer's patients has jumped at such an alarming rate that the Alzheimer's Association (AA) now predicts that in less than 25 years, as many as 22 million people will be diagnosed with the disease worldwide.

HSI has taken a special interest in Alzheimer's disease because we believe there are natural ways to help prevent this epidemic from ever reaching those numbers predicted by the AA. In the past I've promised to keep you abreast of new developments in the research of Alzheimer's prevention, and I've just found a study that confirms the importance of a specific set of nutrients that every person who's reached middle age needs to be aware of.

California recall

As we've seen in previous studies, elevated levels of the amino acid homocysteine have been linked with Alzheimer's disease and other forms of dementia. Considerable research has also demonstrated that foods and supplements rich in vitamins B6, B12, and folic acid help reduce homocysteine levels.

Knowing this, a team of researchers from the University of California (UC) evaluated the relationship of plasma homocysteine concentration and cognitive function of more than 1,700 subjects over the age of 60, all of whom were enrolled in the Sacramento Area Latino Study on Aging. The researchers used a variety of neuropsychological tests specifically designed to study cognitive functions of older people. They also had access to data from blood samples, nutrient intake information, and demographic variables.

After analyzing the cognitive function results against the other data, the UC team found a "modest" association between elevated homocysteine levels and indicators for cognitive decline. They also concluded that the use of B vitamin supplements may provide some protection against cognitive decline among the elderly.

Although these results aren't what you'd call dramatically significant, when compared with other, more conclusive research, the UC study provides confirmation of the existing evidence that B vitamins do in fact provide a measure of prevention against Alzheimer's.

Years of study

Longtime HSI members will recall that we revealed the association between Alzheimer's and elevated homocysteine levels more than a year before it became a hot topic in the mainstream medical journals. In both e-Alerts and Members Alerts we've reported the following test results:

- * 1996 - A study of elderly Americans, published in the American Journal of Clinical Nutrition (AJCN), found that those with high homocysteine levels performed poorly on cognitive tests compared with those who had low homocysteine levels. Low levels of vitamin B12 and folic acid were also associated with low cognitive test scores.
- * 1997 - A 6-year study, (also reported in AJCN) found that subjects who supplemented with vitamins B6 and B12 performed better on cognitive tests, including recall ability.
- * 2002 - A study of more than 1,000 participants in the Framingham Heart Study showed that subjects who had elevated homocysteine levels but no cognitive problems in 1992 were more likely to have an onset of dementia eight years later.

There are many more examples, but you get the picture. We continue to see more and more evidence in different types of trials that certain B vitamins are effective in lowering homocysteine levels, and helping to prevent the onset of Alzheimer's and other forms of age-related dementia.

And of course, any discussion of homocysteine would be incomplete without mentioning that elevated homocysteine levels have also been associated with an increased risk of cardiovascular disease, heart attack, stroke, and Parkinson's disease.

Strong to the "finich"

When homocysteine is not properly metabolized, levels of the amino acid rise. But nutrients such as vitamins B6, B12, and folate help metabolize homocysteine. These nutrients are found in dietary sources such as asparagus, lentils, chickpeas, most varieties of beans, and especially spinach and other leafy green vegetables. But many people don't absorb B vitamins well, so in addition to these food sources,

a B vitamin supplement is often required to lower homocysteine levels.

And according to several studies, supplements of the antioxidant amino acid N-acetylcysteine (NAC) may also lower homocysteine levels. In 2001 we reported on one study that showed how NAC improved cognitive function in patients with probable Alzheimer's Disease. The 24-week study of 47 subjects revealed that those participants who took NAC showed improvement in nearly every outcome measure, without experiencing any negative side effects.

Tell a friend

The next time your doctor takes a blood sample, ask about your homocysteine level and discuss this important issue. (Most doctors consider any level over 12 micromoles per liter to be an elevated homocysteine level.) And if you know someone who has concerns about preventing Alzheimer's and other age-related dementia, please help me on this mission to get the word out.

Share this e-Alert with friends and let them know that lowering homocysteine today could make an important difference in the quality of their lives during the coming years.

http://www.hsibaltimore.com/ea2003/ea_030929_p.shtml

Lancet Neurol, September 1, 2003; 2(9): 539-47.

Reviews

1. Treatment of Alzheimer's disease: current status and new perspectives

Elio Scarpini^a, Philip Scheltens^b and Howard Feldman^c

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Available online 22 August 2003.

Abstract

Alzheimer's disease (AD) is the most common neurodegenerative disorder and the most prevalent cause of dementia with ageing. Pharmacological treatment of AD is based on the use of acetylcholinesterase inhibitors, which have beneficial effects on cognitive, functional, and behavioural symptoms of the disease, but their role in AD pathogenesis is unknown. Other pharmacological therapies are becoming available—including the recently approved drug memantine, an NMDA channel blocker indicated for advanced AD. Here, we review clinical features of the available cholinesterase inhibitors (donepezil, rivastigmine, and galantamine) including their pharmacological properties, the evidence for switching from one agent to another, "head to head" studies, and the emerging evidence for the use of memantine in AD. New therapeutic approaches—including those more closely targeted to the pathogenesis of the disease—will also be reviewed. These potentially disease modifying treatments include amyloid- β -peptide vaccination, secretase inhibitors, cholesterol-lowering drugs, metal chelators, and anti-inflammatory agents.

2. Memantine in moderate-to-severe Alzheimer's disease.

S Bleich, J Wiltfang, and J Kornhuber

N. Engl. J. Med., Aug 2003; 349: 609-10; author reply 609-10. Comment

3. Antinociceptive activity of the N-methyl-D-aspartate receptor antagonist N-(2-Indanyl)-glycinamide hydrochloride (CHF3381) in experimental models of inflammatory and neuropathic pain.

G Villetti, M Bergamaschi, F Bassani, PT Bolzoni, M Maiorino, C Pietra, I Rondelli, P Chamiot-Clerc, M Simonato, and M Barbieri

J. Pharmacol. Exp. Ther., Aug 2003; 306: 804-14. Journal article

[\[Abstract\]](#) [\[Full text\]](#)

Schmerz, August 1, 2003; 17(4): 261-7.

4. [Glutamate antagonists for treatment of neuropathic pain]

[Glutamate antagonists for treatment of neuropathic pain]

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MEDLINE ABSTRACT

An altered glutamatergic transmission within the central nervous system is supposed to be involved in the generation and propagation of neuropathic pain. Results from experimental studies with animal models of neuropathic pain demonstrate that glutamate antagonists have a positive effect on various parameters. Clinical studies with the NMDA-receptor antagonists ketamine, amantadine, **memantine** and dextromethorphan and with the antiepileptics gabapentin and lamotrigine, which reduce presynaptic release of glutamate, have been performed. They have shown that most of these substances can reduce neuropathic pain. Important side effects of the NMDA receptor antagonists

are hallucination and agitation, whereas tiredness and dizziness are the ones of the antiepileptics. Till now, glutamate antagonists are not drugs of first choice for the treatment of neuropathic pain. However, they are an effective alternative in case the established drugs are not helpful or are not tolerated well.

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5. Neurologia, June 1, 2003; 18(5): 255-61.

[Memantine]

JL Molinuevo

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MEDLINE ABSTRACT

Alzheimer's disease (AD) is the most common form of dementia in Western countries. The benefits presently observed with the approved treatments are mainly symptomatic without clear evidence of neuroprotection. N-methyl-D-aspartate (NMDA) receptor antagonists have very extensive therapeutic potential in several central nervous system disorders and can be used as neuroprotective treatment in chronic neurodegenerative diseases and as symptomatic treatment in other neurologic diseases as epilepsy. **Memantine**, an antagonist of the glutamatergic NMDA receptor, has been recently approved for the treatment of advanced AD. Due to its action mechanism, **memantine** is considered a neuroprotective drug, whose utility has been demonstrated in preclinical studies, and a useful symptomatic treatment for AD and vascular dementia. We will review both aspects as well as the basic mechanisms mediating glutamatergic neurodegeneration and the implication of glutamate in cognition.

Publication Type:

6. J Am Geriatr Soc, May 1, 2003; 51(5 Suppl Dementia): S305-13.

Medical management of advanced dementia.

PN Tariot

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MEDLINE ABSTRACT

A cure for Alzheimer's disease (AD) is still far off, and clinicians face the burden of caring for patients at all stages of dementia for the foreseeable future. Those with advanced disease suffer neurological symptoms and signs that include incontinence; problems with gait and mobility; marked cognitive, language, and functional impairment; and in about 90% of patients, significant behavior problems. Dementia precludes the ability to initiate meaningful activities or social interactions. Whether patients are resident in the community or living in a nursing home, this composite reflects a highly complex medical and neuropsychiatric management challenge. Predictable medical conditions also must be addressed (i.e., those that accompany dementia, such as parkinsonism, and those that are prevalent in any aging population, such as hypertension). Clinicians can better address these problems with awareness of current treatment options. Placebo-controlled trials of some psychotropic agents have shown modest favorable effects on behavior problems. Use of acetylcholinesterase inhibitors (AChEIs) to treat cognitive impairment and secondary behavioral symptoms derives primarily from results of placebo-controlled clinical trials. Trials in patients with moderate to severe AD, outpatients as well as nursing home residents, show overall effects similar to those seen in outpatients with milder dementia. Treatment with AChEIs may delay institutional placement. **Memantine** has shown benefit in trials in moderate to severe dementia, although it is not yet approved in the United States. Emerging data have expanded physicians' ability to use pharmacotherapy in patients with advanced dementia. Physicians need to enact the principle that something can be done for our afflicted parents and grandparents.

7. Eur J Clin Pharmacol, May 1, 2003; 59(1): 79-84.

Efficacy, safety and cost of new drugs acting on the central nervous system.

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MEDLINE ABSTRACT

OBJECTIVE: To examine the degree of innovation of the products with indications for CNS diseases approved for the European market through the centralized procedure.

METHODS: This paper examines the documentation available on nine products approved by the European Medicines Evaluation Agency in its first years of activity.

RESULTS: The Committee for Proprietary Medicinal Products approved only five products by consensus (levacetylmethadol, levetiracetam, olanzapine, pramipexole, riluzole). Four were approved by majority (entacapone, **memantine**, rivastigmine, zaleplon). One product received a negative opinion, and five had the application withdrawn before reaching the Committee decision. **CONCLUSIONS:** An analysis of the efficacy and safety profile of these products indicates that few minor therapeutic advances have been achieved in this area. Most approved products cover needs already met, at higher cost, without substantial improvement.

8. N. Engl. J. Med., April 3, 2003; 348(14): 1333-41.

Memantine in moderate-to-severe Alzheimer's disease.

B Reisberg, R Doody, A Stoffler, F Schmitt, S Ferris, HJ Mobius, and Memantine Study Group

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MEDLINE ABSTRACT

BACKGROUND: Overstimulation of the N-methyl-D-aspartate (NMDA) receptor by glutamate is implicated in neurodegenerative disorders. Accordingly, we investigated **memantine**, an NMDA antagonist, for the treatment of Alzheimer's disease. **METHODS:** Patients with moderate-to-severe Alzheimer's disease were randomly assigned to receive placebo or 20 mg of **memantine** daily for 28 weeks. The primary efficacy variables were the Clinician's Interview-Based Impression of Change Plus Caregiver Input (CIBIC-Plus) and the Alzheimer's Disease Cooperative Study Activities of Daily Living Inventory modified for severe dementia (ADCS-ADLsev). The secondary efficacy end points included the Severe Impairment Battery and other measures of cognition, function, and behavior. Treatment differences between base line and the end point were assessed. Missing observations were imputed by using the most recent previous observation (the last observation carried forward). The results were also analyzed with only the observed values included, without replacing the missing values (observed-cases analysis). **RESULTS:** Two hundred fifty-two patients (67 percent women; mean age, 76 years)

from 32 U.S. centers were enrolled. Of these, 181 (72 percent) completed the study and were evaluated at week 28. Seventy-one patients discontinued treatment prematurely (42 taking placebo and 29 taking **memantine**). Patients receiving **memantine** had a better outcome than those receiving placebo, according to the results of the CIBIC-Plus (P=0.06 with the last observation carried forward, P=0.03 for observed cases), the ADCS-ADLsev (P=0.02 with the last observation carried forward, P=0.003 for observed cases), and the Severe Impairment Battery (P<0.001 with the last observation carried forward, P=0.002 for observed cases). Memantine was not associated with a significant frequency of adverse events. **CONCLUSIONS:** Antiglutamatergic treatment reduced clinical deterioration in moderate-to-severe Alzheimer's disease, a phase associated with distress for patients and burden on caregivers, for which other treatments are not available.

Comment in N Engl J Med. 2003 Aug 7;349(6):609-10; author reply 609-10

9. Int Clin Psychopharmacol, March 1, 2003; 18(2): 81-5.

Tolerability of memantine in combination with cholinesterase inhibitors in dementia therapy.

S Hartmann and HJ Mobius

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MEDLINE ABSTRACT

Memantine, a moderate-affinity, uncompetitive N-methyl-D-aspartate (NMDA) receptor antagonist, has been shown to be effective in dementia, including Alzheimer disease (AD). Therefore, its combination with acetylcholinesterase inhibitors (AChEIs) is anticipated. We report a postmarketing surveillance study conducted among German physicians who, during routine clinical practice, treated demented patients with **memantine** in combination with an AChEI. Most of the 158 surveyed patients (mean age, 74 years) were diagnosed with AD but other dementias were included. **Memantine** was prescribed at a wide range of daily doses (median, 20 mg/day) and was combined with donepezil for most patients (84%). Combination therapy was well tolerated for nearly all patients (98%) for an average observation period of 4 months at stable doses of both antidementia agents. No serious adverse drug reaction (ADR) was reported. No ADR or change in blood chemistry was experienced by most patients (96% and 81%, respectively); the six reported ADRs resolved without sequelae and without drug discontinuation. Global clinical status of most patients was judged as improved (54%) or stable (39%) over the observation period. These findings particularly suggest that **memantine** in combination with AChEIs is safe and well tolerated

10. *Drugs Aging*, January 1, 2003; 20(6): 465-76.

Memantine.

B Jarvis and D Figgitt

Adis International Limited, Auckland, New Zealand.



The image shows a screenshot of a web interface with a grey background. At the top, there is a yellow box with the word "SERVICES" in blue. Below this, there are two blue links: "Add to Personal Archive" and "Download to Citation Manager", each preceded by a small orange triangle. Below these links is another yellow box with the word "MEDLINE" in blue. Underneath, there is a blue link "Related Articles in Medline" preceded by an orange triangle. Below this link, the text "Articles in Medline by Author:" is displayed. At the bottom, there are two more blue links: "Jarvis, B" and "Figgitt, D", each preceded by an orange triangle.

MEDLINE ABSTRACT

black triangle **Memantine**, an uncompetitive antagonist with moderate affinity for NMDA receptors, demonstrates voltage-dependency and relatively fast on/off receptor kinetics. black triangle **Memantine** 20 mg/day significantly slowed the rate of deterioration in outpatients with moderate to severe Alzheimer's disease in a 28-week US randomised, double-blind, placebo-controlled, multicentre study. black triangle **Memantine** 10 mg/day improved measures of dementia in care-dependent inpatients with Alzheimer's disease or vascular dementia in a 12-week randomised, double-blind study. Significantly more **memantine** than placebo recipients were responders according to Clinical Global Impression of Change scores and the Behavioural Rating Scale for Geriatric Patients Care Dependence subscale. black triangle **Memantine** 20 mg/day significantly improved cognition-related outcomes (cognitive subscale of the Alzheimer's Disease Assessment Scale) in patients with vascular dementia in two 28-week randomised, double-blind, placebo-controlled, multicentre trials. No statistically significant between-group difference was seen in other primary endpoints. black triangle Adverse events (incidence in **memantine** recipients greater than in placebo recipients) occurring in patients with moderately severe to severe dementia included diarrhoea, insomnia, dizziness, headache and hallucination

11. Brain Res, December 20, 2002; 958(1): 210-21.

Neuroprotection by memantine against neurodegeneration induced by beta-amyloid(1-40).

JJ Miguel-Hidalgo, XA Alvarez, R Cacabelos, and G Quack

Department of Psychiatry and Human Behavior, University of Mississippi Medical Center, Jackson, MS, USA. jmiguel-hidalgo@psychiatry.umsmed.edu

12. Int Clin Psychopharmacol, November 1, 2002; 17(6): 297-305.

A double-blind, placebo-controlled multicentre study of memantine in mild to moderate vascular dementia (MMM500).

G Wilcock, HJ Mobius, A Stoffler, and MMM 500 group

Bristol University, Department of Care of the Elderly, Frenchay Hospital, Bristol, UK.

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MEDLINE ABSTRACT

The aim of the reported trial was to investigate the safety and efficacy of **memantine** in mild to moderate vascular dementia (VaD). This was a 28-week, double-blind, parallel, randomized controlled trial of **memantine** 20 mg daily versus placebo which was conducted in 54 centres in the UK. **Memantine** is a uncompetitive, moderate affinity N-methyl-D-aspartate receptor antagonist. Patients with a diagnosis of probable VaD and Mini Mental State Examination total scores between 10 and 22 were eligible for inclusion. Primary efficacy parameters were the Alzheimer's Disease Assessment Scale-Cognitive Subscale (ADAS-cog) and the Clinical Global Impression of Change (CGI-C). A total of 579 patients were randomized and 548 patients with at least one post-baseline efficacy assessment qualified for the intent-to-treat analysis. At endpoint, **memantine** was shown to improve cognition relative to placebo in VaD: the change of ADAS-cog from baseline differed by a mean of -1.75 points (95% confidence intervals -3.023 to -0.49) and a median of 2 points between the two groups, while CGI-C ratings showed no significant differences between treatment groups. A total of 77% of all **memantine**-treated patients experienced adverse event, versus 75% of the placebo-treated patients, dizziness being the most frequent adverse event (11% versus 8%, respectively). **Memantine** was well tolerated and safe

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MEDLINE ABSTRACT

Progressive neuronal loss and cognitive decline in Alzheimer's disease (AD) might be aggravated by beta-amyloid-enhanced excitotoxicity. **Memantine** is an uncompetitive NMDA receptor antagonist under clinical development for the treatment of AD. **Memantine** has neuroprotective actions in several in vitro and in vivo models. In the present study, we determined whether **memantine** protected against beta-amyloid induced neurotoxicity and learning impairment in rats. Twenty Sprague-Dawley rats received vehicle or vehicle plus **memantine** (steady-state plasma concentrations of 2.34 ± 0.23 μM , $n=10$) s.c. by osmotic pump for 9 days. After 2 days of treatment, 2 μl of water containing beta-amyloid 1-40 [A β (1-40)] were injected into the hippocampal fissure. On the ninth day of treatment, animals were sacrificed, and morphological and immunohistochemical techniques were used to determine the extent of neuronal degeneration and astrocytic and microglial activation in the hippocampus. Psychomotor activity and spatial discrimination were tested on the eighth day of treatment. A β (1-40), but not water, injections into hippocampus led to neuronal loss in the CA1 subfield, evidence of widespread apoptosis, and astrocytic and microglial activation and hypertrophy. **Memantine** treated animals had significant reductions in the amount of neuronal degeneration, pyknotic nuclei, and GFAP immunostaining as compared with vehicle treated animals. These data suggest that **memantine**, at

therapeutically relevant concentrations, can protect against neuronal degeneration induced by beta-amyloid

13. <http://216.247.57.19/memantine2.htm>

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treatment begun in a foreign country.

14.

EPIC4HEALTH



Omega-3 and Alzheimer's

A recent study published in July 2003 in Archives of Neurology showed that people who ate Omega 3 rich fish such as salmon once a week or more had a substantially lower risk of Alzheimer's disease. In fact, the seven-year study of 815 nursing home residents found those who reported eating fish at least once a week had a 60 percent lower risk of Alzheimer's compared to those who rarely or never ate fish.

This new finding is in sync with a growing body of scientific evidence that suggests people can reduce their risk of developing a number of killer diseases, such as heart disease, cancer and now Alzheimer's, **if they ate a healthier diet - one rich in Omega 3 oils from fish, plus plenty of fresh fruits and vegetables.**

In an accompanying editorial, Robert Friedland, M.D. of Case Western Reserve University School of Medicine in Cleveland, Ohio, said a healthy diet containing fish could help ward off a host of ailments, not just Alzheimer's, though he warned of toxins such as mercury tainting some fish.

Most health experts agree that eating fish high in Omega 3 is a good idea, but they also warn that some people, particularly pregnant women and young children, should avoid fish high in methyl mercury, a harmful contaminant found in some fish. Swordfish, shark, tuna and other large predatory fish can contain lots of mercury, while salmon, flounder and cod generally do not have as much.

Dr. Friedland wrote: *"A high antioxidant/low saturated fat diet pattern with a greater amount of fish, chicken, fruits, and vegetables and less red meat and dairy products is likely to lower the risk of Alzheimer's disease, as well as that for heart disease and stroke".*

Dr. Friedland went on to say that fish oil supplements, **which were not considered in this study**, can also be a good source of omega-3 fatty acids.

If the mercury content in the fish you are eating is a concern or if you are just not eating enough omega 3 rich fish, you may want to consider our Omega 3 Enteric Coated Softgels. **The enteric coating means no fishy after taste! More importantly, our fish oil partners are world leaders in sourcing raw material fish oils for nutritional supplement products. They have tight purchasing parameters related to pcb's and heavy metals and will not use oils for further refining if they find these types of materials in them. The strict manufacturing processes including molecular distillation ensure that these elements are not found in the finished oil. In addition, independent testing of our products insure our compliance with California Proposition 65 related to heavy**

15. Drug and vitamin E slow Alzheimer's

URL of this page: http://www.nlm.nih.gov/medlineplus/news/fullstory_13815.html (*this news item will not be available after 09/27/2003)

United Press International
Thursday, August 28, 2003

COLUMBUS, Ohio, Aug 27, 2003 (United Press International via COMTEX) -- Combining vitamin E and a drug used to treat moderate dementia might slow the progression of Alzheimer's disease, a new Ohio State University study reports.

Researchers found after a year of treatment with vitamin E and the drug donepezil, which is sold under the brand name Aricept, people with Alzheimer's disease performed much better on tests of cognitive ability than did people who hadn't taken either substance.

"There were notable cognitive differences even after three years of combined therapy," said David Beversdorf, the study's senior author.

Beversdorf studied Alzheimer's patients who took daily doses of both vitamin E and donepezil. The participants took a cognitive-abilities test each year during the three-year study. Test scores were compared to those of Alzheimer's patients who took the same test prior to 1996, before donepezil and similar drugs were available and before vitamin E was touted as having a role in disease prevention.

The decline in cognitive test scores of patients who had not taken either agent was three times greater after a year than the decline in scores of patients taking the combined therapy.

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16. Alternative Treatments for Alzheimer's

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Several herbal remedies and other dietary supplements are promoted as effective treatments for Alzheimer's disease and related disorders. Claims about the safety and effectiveness of these products, however, are based largely on testimonials, tradition, and a rather small body of scientific research. The rigorous scientific research required by the U.S. Food and Drug Administration for the approval of a prescription drug is not required by law for the marketing of dietary supplements.

Concerns about alternative therapies

Although many of these remedies may be valid candidates for treatments, there are legitimate concerns about using these drugs as an alternative or in addition to physician-prescribed therapy:

- **Effectiveness and safety are unknown.** The maker of a dietary supplement is not required to provide the U.S. Food and Drug Administration (FDA) with the evidence on which it bases its claims for safety and effectiveness.
- **Purity is unknown.** The FDA has no authority over supplement production. It is a manufacturer's responsibility to develop and enforce its own guidelines for ensuring that its products are safe and contain the ingredients listed on the label in the specified amounts.
- **Bad reactions are not routinely monitored.** Manufacturers are not required to report to the FDA any problems that consumers experience after taking their products. The agency does provide voluntary reporting channels for manufacturers, health care professionals, and consumers, and will issue warnings about products when there is cause for concern.
- Dietary supplements can have serious interactions with prescribed medications. No supplement should be taken without first consulting a physician.

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Ginkgo biloba

Ginkgo biloba is a plant extract containing several compounds that may have positive effects on cells within the brain and the body. *Ginkgo biloba* is thought to have both antioxidant and anti-inflammatory properties, to protect cell membranes, and to regulate neurotransmitter function. *Ginkgo* has been used for centuries in traditional Chinese medicine and currently is being used in Europe to alleviate cognitive symptoms associated with a number of neurological conditions.

In a study published in the *Journal of the American Medical Association* (October 22/29, 1997), Pierre L. Le Bars, MD, PhD, of the New York Institute for Medical Research, and his colleagues observed in some participants a modest improvement in cognition, activities of daily living (such as eating and dressing), and social behavior. The researchers found no measurable difference in overall impairment.

Results from this study show that ginkgo may help some individuals with Alzheimer's disease, but further research is needed to determine the exact mechanisms by which *Ginkgo* works in the body. Also, results from this study are considered preliminary because of the low number of participants, about 200 people.

Few side effects are associated with the use of *Ginkgo*, but it is known to reduce the ability of blood to clot, potentially leading to more serious conditions, such as internal bleeding. This risk may increase if *Ginkgo biloba* is taken in combination with other blood-thinning drugs, such as aspirin and warfarin.

Currently, multicenter trial with about 3,000 participants is investigating whether *Ginkgo* may help prevent or delay the onset of Alzheimer's disease or vascular dementia.

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Huperzine A

Huperzine A is a moss extract that has been used in traditional Chinese medicine for centuries. Because it has properties similar to those of FDA-approved Alzheimer medications, it is promoted as a treatment for Alzheimer's disease.

Evidence from small studies show that the effectiveness of huperzine A may be comparable to that of the approved drugs. Large-scale trials are needed to better understand the effectiveness of this supplement.

Because huperzine A is a dietary supplement, it is unregulated and manufactured with no uniform standards. If used in combination with FDA-approved Alzheimer drugs, an individual could increase the risks of serious side effects.

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Phosphatidylserine

Phosphatidylserine (pronounced *FOS-fuh-TIE-dil-sair-een*) is a kind of lipid, or fat, that is the primary component of cell membranes of neurons. In Alzheimer's disease and similar disorders, neurons degenerate for reasons that are not yet understood. The strategy behind the possible treatment with phosphatidylserine is to shore up the cell membrane and possibly protect cells from degenerating.

The first clinical trials with phosphatidylserine were conducted with a form derived from the brain cells of cows. Some of these trials had promising results. However, most trials were with small samples of participants.

This line of investigation came to an end in the 1990s over concerns about mad cow disease. There have been some animal studies since then to see whether phosphatidylserine derived from soy may be a potential treatment. A report was published in 2000 about a clinical trial with 18 participants with age-associated memory impairment who were treated with phosphatidylserine. The authors concluded that the results were encouraging but that there would need to be large carefully controlled trials to determine if this could be a viable treatment.

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Homocysteine and Dementia

Seshadri and colleagues (Feb. 14 issue)¹ report that high homocysteine levels are a risk factor for Alzheimer's disease. The effect of homocysteine on brain tissue is influenced by the absence within this tissue of two of the major metabolic routes for the elimination of homocysteine: betaine-mediated conversion and transsulfuration.^{2,3} Consequently, under conditions of folate deprivation, homocysteine can be eliminated only by export from the neuron. Increased export is problematic, however, as the authors point out, since homocysteine activates *N*-methyl-D-aspartate receptors and potentiates glutamate excitotoxicity.⁴ Minimizing homocysteine export may therefore be critical . . . ([Click here for the full](#))