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Guest Editors: Candace N. Farley, Pharm.D., Lauren Hofer, Pharm.D. Candidate and Mary C. Huynh, Pharm.D. Candidate



November is National Alzheimer Disease Month



10 Warning Signs of Alzheimer's

- 1.) **MEMORY LOSS:** A person forgetting recently learned information is one of the most common early signs of dementia. The person is more forgetful and is unable to recall the information later.
- 2.) **DIFFICULTY PERFORMING FAMILIAR TASKS:** People with dementia often find it hard to plan or complete everyday tasks. Individuals may lose track of the steps involved in placing a telephone call, preparing a meal, or playing a familiar game.
- 3.) **PROBLEMS WITH LANGUAGE:** People with Alzheimer's disease (AD) often forget simple words or substitute unusual words into their speech or writing making them hard to understand.
- 4.) **DISORIENTATION TO TIME AND PLACE:** People with Alzheimer's disease can become lost in familiar places like their own neighborhood. They can forget where they are or how they got there; they often will find it difficult to find their way home after brief walks.
- 5.) **POOR OR DECREASED JUDGMENT:** Those with Alzheimer's may dress inappropriately, wearing several layers on a warm day or little clothing in the cold. Also poor judgment may be shown by giving away large sums of money to charities or telemarketers.
- 6.) **PROBLEMS WITH ABSTRACT THINKING:** Someone affected with Alzheimer's disease may have unusual difficulty performing complex mental tasks, like forgetting what numbers or alphabets are for and how they are used.

7.) **MISPLACING THINGS:** A person with Alzheimer's disease may put things in unusual places: an iron in the freezer or a wristband in the sugar bowl.

8.) **CHANGES IN MOODS OR BEHAVIORS:** Rapid mood swings- from calm to tears to anger-for no apparent reason occurs commonly in people with Alzheimer's

9.) **CHANGES IN PERSONALITY:** The personalities of people with dementia can change dramatically. They may become extremely confused, suspicious, fearful or dependent on a family member.

10.) **LOSS OF INITIATIVE:** A person with Alzheimer's disease may become very passive, sitting in front of a TV for hours, sleeping longer than usual, or not wanting to do usual activities of pleasure.

Alzheimer's Association [homepage on the Internet]: Warning Signs of Alzheimer's; [updated 2008 October 31, cited 2008 Oct 31]. Available from: http://www.alz.org/alzheimers_disease_symptoms_of_alzheimers.asp

Traditional Drug Therapy For Alzheimer's Disease

Limited therapy exists for the treatment of Alzheimer's. While therapy may improve cognitive function, it is important to remember that these therapies do not stop or reverse the degenerative process.

- Cognitive loss is associated with the depletion of acetylcholine, thus **acetylcholinesterase inhibitors** are utilized to increase the concentration of acetylcholine in the brain.¹ FDA approved acetylcholinesterase inhibitors are Aricept® (donepezil), Razadyne® (galantamine), and Exelon® (rivastigmine).
- The amino acid glutamate has also been shown to be involved in the development of AD via overstimulation of the N-methyl-D-aspartate (NMDA) receptor.² The other FDA approved drug is Namenda® (memantine), an **NMDA-receptor antagonist**. By blocking the receptor, Namenda® blocks the action of glutamate.
- While not approved for the treatment of AD, **antipsychotics** are often used in the disease to treat the behavioral symptoms, such as agitation, associated with the disease.¹ Second generation atypical antipsychotics (Zyprexa® [olanzapine], Risperdal® [risperidone]) are recommended over traditional antipsychotics due to reduced risk of extrapyramidal side effects, however, caution is still warranted in the elderly population.

1. Drugs for Cognitive Loss and Dementia. Treatment Guidelines from the Medical Letter. © The Medical Letter Inc. 2007; 5(54):1-10.

2. Lexi-Comp [database online]. Hudson, OH: Lexi-Comp, Inc. Copyright © 1978-2007. <http://www.crlonline.com/crlsql/servlet/crlonline>. Cited 2008 Nov 6.

NEW DRUG INFORMATION, and other related stuff...

- **Can I get that in a combo?** ... A recently published study suggests that combining two Alzheimer's drugs is more effective than monotherapy. The study evaluated 382 patients with AD who were assigned to one of three treatment groups: 144 received no treatment (NO-RX), 122 received cholinesterase inhibitor monotherapy (CI), and 116 received combination CI + memantine therapy (COMBO). Cognition and function were assessed at 6 month intervals (mean follow-up = 30 months) using the Blessed Dementia Scale (BDS) and the Activities of Daily Living scale (ADL), respectively. Preliminary findings revealed lower mean annual rates of deterioration in the COMBO group. Investigators' concluded that combination therapy may significantly delay cognitive and functional decline in patients with AD.

Atri A, Shaughnessy L, Locascio JJ. Long-term Course and Effectiveness of Combination Therapy in Alzheimer's Disease. *Alzheimer Dis Assoc Disord.* 2008;22(3): 209-221.



On the horizon ... An experimental drug called **Remember® (methylthioninium chloride or MTC)**, developed by TauRx, a Singapore-based company, demonstrated that it delayed the progression of Alzheimer's disease by inhibiting the aggregation of tau proteins responsible for the "tangles," in the description "plaques and tangles" associated with Alzheimer's disease.^{1,2} Results from this unpublished phase II trial are promising, and talks about a phase III trial are in development.²

Another drug up for discussion was **dimebon**, an old antihistamine originally developed in Russia.² A six-month, open-label, phase II trial demonstrated that the agent may help improve mitochondrial function.

These preliminary results were discussed at the 2008 Alzheimer's Association International Conference on Alzheimer's Disease (ICAD 2008) in Chicago.²

¹Park A. Alzheimer's Research Holds Promise. *Time*. 2008 July 31.

<http://www.time.com/time/health/article/0,8599,1828083,00.html>

²International Conference on Alzheimer's Disease: Highlights of Research Findings. Alzheimer's Association.

http://www.alz.org/icad/documents/2008_ICADhighlights.pdf



Perispinal etanercept ... A six month trial was conducted on 12 patients with mild to severe dementia where they were treated with 25 – 50 mg of perispinal etanercept weekly.¹ Participants underwent neurocognitive assessments monthly, which included tests such as: Logical Memory I and II, Boston Naming Test (BNT), and Wechsler Memory Scale-Abbreviated. The pilot study revealed that all measures of cognition were significantly improved ($p < 0.05$), except for two tests (BNT and the Comprehensive Trail Making Test). These findings were ... consistent with the evidence presented from two case reports. Perispinal etanercept may result in the improvement of behavior, comprehension and conversational abilities, and may be useful for patients with variants of frontal lobe Alzheimer's disease or dementia originating from the frontotemporal region.

Soon after the study was published, the Alzheimer's Association released a statement embracing the recent findings yet discouraging healthcare professionals from prescribing etanercept in this off-label manner.² The association feared that patients, family members and physicians may prematurely have a field day on the basis of these preliminary results.

¹Tobinick EL, Gross H. Rapid improvement in verbal fluency and aphasia following perispinal etanercept in Alzheimer's disease. *BMC Neurol*. 2008;8:27.

²Alzheimer's Association statement on a newly published study of Etanercept (Enbrel) for Alzheimer's Disease. Alzheimer's Association. 2008 July 31. [Accessed 11/04/08 http://www.alz.org/news_and_events_14053.asp]

FROM THE MEDICAL LITERATURE ...



Exercise does more than a body good...Recent research has shown that physical activity can improve cognitive function and slow the decline of dementia in people at risk of developing Alzheimer's Disease (AD). A single site trial in Perth, Australia set out to determine whether or not physical activity slows the decline of cognitive impairment in older adults at risk of developing AD. Participants were involved in a 24 week home based physical activity program and were followed for 18 months thereafter. The investigators were studying the change in the cognitive subscale of the Alzheimer Disease Association Scale (ADAS-cog). They found that after the 24 week study period, patients in the study group increased their level of activity. Patients in the study group had better ADAS-cog scores, as well as better delayed recall and clinical dementia ratings than the control group. Investigators

determined that moderate activity for approximately 20 minutes per day would improve cognition in older adults at risk of AD.

Lautenschlager N, Cox KL, Flicker L, Foster JK, van Bockxmeer FM, Xiao J, et al. Effect of Physical Activity on Cognitive Function in Older Adults at Risk for Alzheimer Disease. *JAMA*. 2008; 300(9): 1027-1037.

▪ **High Dose Vitamins and Cognitive Decline...** JAMA recently published an 18-month trial studying the effects of high dose Vitamin B supplements on the cognitive function in Alzheimer's patients. Previous research has found that patients with Alzheimer Disease (AD) have elevated levels of homocysteine, which may contribute to the disease by vascular and endothelial decline. Folic acid and vitamins B₆ and B₁₂ are cofactors in the homocysteine pathway, and can reduce the amount of homocysteine in the body. This study conducted by the Alzheimer Disease Cooperative Study was to determine the efficacy and safety of Vitamin B supplementation in AD by evaluating the change in the cognitive subscale of the Alzheimer Disease Association Scale (ADAS-cog). The active study group received 5 mg/day of folic acid, 1 mg/day of vitamin B₁₂, and 25 mg/day of vitamin B₆ for 18 months. After 18 months, the levels of homocysteine declined, but the rate of change in the ADAS-cog score did not differ significantly between the active treatment and placebo groups. There was also no significant decline in the Clinical Dementia Rating sum of boxes. The study concluded that the recommendation of supplementation with B vitamins in patients with AD with normal levels of B vitamins could not be supported.

Aisen PS, Schneider LS, Sano M, Diaz-Arrastia R, van Dyck CH, Weiner MF, et al. High Dose B Vitamin Supplementation and Cognitive Decline in Alzheimer Disease A Randomized Controlled Trial. *JAMA*. 2008; 300(15):1774-1783.

FROM THE LAY LITERATURE ...

▪ **A Promising New Vitamin...** Previous studies¹ have investigated the use of Vitamins B₆ and B₁₂ in cognitive decline in Alzheimer Disease (AD) patients and have been inconclusive in the results. Enrollment in a new study investigating the use of Vitamin B₃ (nicotinamide) on memory function in AD has begun.² Studies on mice found that the engineered forgetful mice who took the vitamin did well in memory testing, but researchers are unsure if it will have the same effect in humans. It is proposed that the vitamin clears the tangles of the tau protein in brain cells.²

1. Aisen PS, Schneider LS, Sano M, Diaz-Arrastia R, van Dyck CH, Weiner MF, et al. High Dose B Vitamin Supplementation and Cognitive Decline in Alzheimer Disease A Randomized Controlled Trial. *JAMA*. 2008; 300(15):1774-1783.
2. Dotinga R. Vitamin Holds Promise for Alzheimer's Disease. *Washington Post*. November 5, 2008. Cited 2008 Nov 5.
<http://www.washingtonpost.com/wp-dyn/content/article/2008/11/05/AR2008110502796.html>

▪ **Scientists Spot 4 New Alzheimer's Genes...** A team of researchers from Massachusetts General Hospital-MassGeneral Institute for Neurological Disease, part of the Alzheimer's Genome Project (AGP), have identified four new genes linked to late-onset Alzheimer's disease.^{1,2} The strongest marker was on chromosome 14.² Another identified is known to cause spinocerebellar ataxia, which is involved in nerve cell death, while another is involved in the innate immune system.² Identification of these genes may lead to new, or more aggressive, therapies to slow, stop, or reverse the effects of the disease.

1. Roscow D. Breakthrough Mapping of Alzheimer's Genome Helps ID Four New Suspect Genes. MarketWatch.com. Copyright (C) 2008 PR Newswire [updated 2008 Oct 30, cited 2008 Nov 5] Available at <http://www.marketwatch.com/news/story/Breakthrough-Mapping-Alzheimers-Genome-Helps/story.aspx?guid=%7BB9748602-8F3F-4933-993B-DB7C9BF80515%7D>
2. Priedt R. Scientists Spot 4 New Alzheimer's Genes. HealthDay News. [Oct 30,2008. cited November 5, 2008.] Available at: <http://www.healthday.com/Article.asp?AID=620776>.

- **Benefits of Light and Melatonin ...** *JAMA* recently published a study analyzing the long term effects of bright light and melatonin on cognitive and noncognitive function. The study included 189 residents from 12 different group care facilities in the Netherlands from 1999 to 2004. The participants were randomly assigned to receive long term daily treatments of bright light or dim light and melatonin 2.5 mg or placebo in the evening. Illumination therapy was well tolerated by study participants and modestly reduced changes in mood, behavior, cognitive deterioration, functional abilities and sleep. Improvements in sleep onset and duration were reported with melatonin therapy. It was noted that combination therapy (light + melatonin) is recommended to suppress the adverse mood effects. Riemersma-van der Lek RF, Swaab DF, Twisk J, et al. Effect of Bright Light and Melatonin on Cognitive and Noncognitive Function in Elderly Residents of Group Care Facilities: A randomized controlled trial. 2008;299(22):2642-2655.

Reviews of Note ...

- Qaseem A, Snow V, Cross JT, et al. Current Pharmacologic Treatment of Dementia: A Clinical Practice Guideline from the American College of Physicians and the American Academy of Family Physicians. *Ann Intern Med.* 2008;148:370-378.
- Raina P, Santaguida P, Ismaila A, et al. Effectiveness of Cholinesterase Inhibitors and Memantine for Treating Dementia: Evidence Review for a Clinical Practice Guideline. *Ann Intern Med.* 2008;148:379-397.

Ways to Raise Awareness

- Alzheimer wristband – make a donation and receive the purple “A reason to hope” wristband
- Holiday cards – designed by people with AD
- Alzheimer’s disease awareness postage stamp – newly available since October 17, 2008, the U.S. Postal Service has added AD to its long tradition of spotlighting health and social services
- Visit http://www.alz.org/join_the_cause_join_the_cause.asp to view these and other ways to join the cause.

For more information on Alzheimer’s Disease, check out these helpful resources

- Alzheimer’s Association <http://www.alz.org/index.asp>
- National Institute on Aging – Alzheimer’s Disease Genetics Fact Sheet <http://www.nia.nih.gov/Alzheimers/Publications/geneticsfs.htm>

Other awareness events for November

- American Diabetes Month
- National Healthy Skin Month
- COPD Awareness Month
- Great American Smokeout (11/16)
- Pulmonary Hypertension Awareness Month
- Lung Cancer Awareness Month
- Prostate Cancer Awareness Month
- Pancreatic Cancer Awareness Month

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Bernie R. Olin, Pharm.D., Director