AU InforMed

Volume 7 Number 14 (Issue 222) *Monday, November 2, 2009*

Guest Editors: Alison Baker, Pharm. D. Candidate and Leeann Cline, Pharm. D. Candidate

Key Inforbits

- About Alzheimer's Disease
- Warning Signs and Screening Tools
- Non-pharmacologic Therapy
- Herbal Remedies
- Pharmacologic Therapy
- From the Medical Literature

November is...

Alzheimer's Disease Awareness Month

About Alzheimer's Disease (AD)

Alzheimer's Disease (AD) is a gradually progressive dementia characterized by loss of cholinergic neurons in the Central Nervous System (CNS). It affects approximately 4.5 million Americans, and is the most common cause of dementia. The greatest risk factor for AD is increasing age, affecting 53% of those between the age of 75 and 84. Onset may occur as early as age 40 (early-onset) but is more common after age 65 (late-onset AD). The etiology of AD is unknown, so current therapies do not cure or stop disease progression. The most important interventions for AD are nondrug therapy and social support for the patient and family members.[1]

1. *Slattum PW, Swerdlow RH, Hill AM. Alzheimer's Disease. In: Dipiro JT, Talbert RL, Yee GC, Wells BG, Posey LM. Pharmacotherapy A Pathophysiologic Approach. 7th ed. NY: McGraw-Hill, 2008, p. 1051-1052.*

HEED THE WARNINGS!!

There are 10 warning signs identified by the Alzheimer's Association that may indicate early AD. These signs are different from typical age related changes in that they are much more severe or frequent than age-related changes in mental capability or cognitive function.[1,2]

1. Memory changes that disrupt daily life
   Trouble with short term memory, forgetting dates or events, asking for people to repeat information .
2. Challenges in planning or solving problems
   Difficulty concentrating, keeping track of personal finances, manipulating numbers or following a basic recipe.
3. Difficulty completing familiar tasks
   Trouble remembering rules to a game, driving to a familiar location, or managing your household budget.
4. Confusion with time or place
   Loosing track of the season, month, day, time, or forgetting how you got to a particular place.
5. Trouble understanding visual images or spatial relationships
   Difficulty reading, judging distance when driving or playing sports, determining color or contrast.
6. New problems with language
   Trouble following a conversation, repeating one's self, calling things by the wrong name.

7. Misplacing things

   Putting things in unusual places, loosing items, accusing others of stealing your belongings.

8. Decreased or poor judgment

   Poor decision with money, paying less attention to hygiene and grooming.

9. Withdrawal from work or social activities

   Removing one's self from once-pleasurable activities, trouble completing hobbies, social avoidance.

10. Changes in mood and personality

    Increasing confusion, suspicion, depression, fear, anxiety, irritability and frustration.

1. *Alzheimer's Association [Internet]. Chicago: Alzheimer's Association National Office; c2009. 10 signs of Alzheimer's; 2009 Sept 14[cited 2009 Sept 16]; [about 5 screens]. Available from:http://www.alz.org/alzheimers_disease_10_signs_of_alzheimers.asp*
2. *Helpguide: understand, prevent and resolve life's challenges [Internet]. Santa Monica: Wise and healthy aging; c2009. Alzheimer's disease symptoms and stages; 2009 April [cited 2009 Sept 16]; about 4 screens. Available from: http://www.helpguide.org/elder/alzheimers_disease_symptoms_stages.htm*

Screening tools

This table provides a brief summary of the screening tools used to test for AD. As there is no way to diagnose Alzheimer's Disease in the absence of a brain biopsy, clinicians rely on tools such as the MMSE and clock scores to help them diagnose.

Name of Measurement	Number of items; Time required; Maximum score	Cognitive Functions Assessed
MMSE (Mini-Mental State Exam)	19 items; 10 minutes; Max score = 20	Orientation, registration, attention and calculation, short term verbal recall, naming, repetition, 3-step command, reading, writing, visuospatial
SLUMS (St. Louis University Mental Status Examination)	11 items; 7 minutes; Max score = 30	Orientation, verbal recall, calculation, naming, attention, executive function (Note: includes clock drawing)
Clock Drawing	5 items; no time limit; Max score= 5	Memory, information processing, vision, spatial orientation.
BOMC (Blessed orientation memory-concentration test)	6 items; 3 minutes; Max score = 28	Orientation, concentration, short term verbal recall

Adapted from *Qaseem A et al. Current pharmacologic treatment of dementia: a clinical guideline from the American College of Physicians and the Academy of Family Physicians. Ann Intern Med. 2008 Mar 4;148 (5):370-377. Available at: www.annals.org*

Non-pharmacologic treatments

Current non-pharmacologic treatments for the management of AD are aimed at helping with sleep disturbances, wandering, urinary incontinence, agitation, and aggression. These include:

- ✓ Maintaining regular times for meals, bed time and waking
- ✓ Seek morning sunlight exposure
- ✓ Avoid alcohol, nicotine and caffeine
- ✓ Regular daily exercise no later than 4 hours prior to bedtime
- ✓ Avoid giving cholinesterase inhibitors before bed
- ✓ Discourage lying in bed if the person is awake

These measures are designed to alleviate some of the common issues related to Alzheimer's disease, but are not a substitute for pharmacologic therapy for treating the underlying disease process.

Herbal Remedies

Some common herbal remedies touted to help manage AD include gingko biloba, vitamin E and Huperzine A.

- ✓ Gingko Biloba: Ginkgo interacts with the CYP system so there is high potential for drug interactions and it has been shown to increase the risk for bleeding when coadministered with other antiplatelet drugs. Ginkgo is perhaps the most widely studied herbal remedy for AD and is shown to have some modest benefit in improving cognition in patients with AD. However, its effects are less as the disease progresses[1,2].

- ✓ Huperzine A: Due to its cholinesterase-like mechanism of action, this herbal should not be used along with prescription therapy for Alzheimer's disease. Studies with huperzine A have only been conducted in China and those studies did not find a conclusive role for huperzine A in the treatment of the disease despite its unique mechanism of action relative to other herbal remedies for AD [1,3].

- ✓ Vitamin E (tocopherol): Vitamin E may interact with warfarin and statins causing serious side effects. In studies, some correlation is seen between AD and low serum vitamin E levels. However, studies show no significant improvements in cognitive function in patients treated with 2000 units per day compared to those treated with donepezil or placebo[1,3].

1. *Drug Facts and Comparisons (eFacts) [AUHSOP Intranet]. St. Louis: Wolters Kluwer Health [updated 2009, cited 2009 Sept 16]. [about 3 p.]. Available from http://online.factsand comparisons.com/index.aspx?*
2. *University of Maryland Medical Center. Baltimore: c2009. Ginkgo Biloba; 2007 Jan 26 [cited 2009 Sept 17];[about 7 screens. Available from http://www.umm.edu/altmed/articles/ginkgo-biloba-000247.htm*
3. *Natural Medicines Comprehensive Database [AUHSOP Intranet]. Stockton, CA: Huperzine A, Ginkgo Biloba [updated Mar 11, 2009, cited 2009 Sept 10]. [about 3 p.] Available from http://www.naturaldatabase.com/(S(vpiolengdtoses3cs2kiho45))/home.aspx?s=ND&referer=web99s.auburn.edu/web99/pharmacy*

Pharmacologic Treatment of AD[1,2,3]

Drug Class	Drug Names	Mechanism	Indications	Doses	ADRs
Cholinesterase Inhibitors 	Donepezil (Aricept) Rivastigmine (Exelon) Galantamine (Razadyne)	Reversibly and noncompetitively inhibit central acetylcholinesterase, which results in increased concentrations of acetylcholine in the synapses of the CNS	First-line therapy for mild or moderate AD (Aricept is also approved in severe AD)	Aricept: 5-10 mg Qday Exelon: 3-6 mg BID Exelon patch: 4.6-9.5 mg/24 hr Razadyne ER: 8-24 mg Qday Razadyne IR: 4-24 BID	Dizziness, headache, nausea, and vomiting
NMDA Receptor Inhibitor	Memantine (Namenda)	Antagonist at NMDA glutamate receptors (antiglutamatergic action)	Add-on therapy in moderate to severe AD and can also be used as monotherapy	Initial dose of 5 mg Qday, titrated in 5 mg increments to 5 mg BID, then 5 mg and 10 mg as separate doses, then 10 mg BID	Hypertension, dizziness, and headaches

1. Drug Facts and Comparisons (eFacts) [AUHSOP Intranet]. St. Louis: Wolters Kluwer Healt [updated 2009, cited 2009 Sept 28]. [about 3 p.]. Available from http://online.factsand comparisons.com/index.aspx?
2. DiPiro JT, Talbert RL, Yee GC, Matzke GR, Wells BG, Posey LM.Pharmacotherapy: a pathophysiologic approach. 7th ed. New York City: McGraw-Hill; 2008. p.1051-1063.
3. Lexi-Comp Electronic Edition. Hudson, OH: Lexi-Comp, Inc. Copyright ©1978-2007. http://www.crlonline/crsql/servlet/crlonline.

From the Medical Literature….

Doody RS, Gavrilova S, Sano M, et al. Effect of dimebon on cognition, activities of daily living, behavior, and global function in patients with mild-to-moderate Alzheimer's disease: a randomized, double-blind, placebo-controlled study. Lancet [Internet]. 2008 July 19 [cited 2009 Sept 16]; 372:207-15

- This is a Russian-based study that discusses the use of dimebon, a non-selective antihistamine that was pulled from their market once more selective agents were introduced. Researchers recently discovered that the compound is a weak acetylcholinesterase inhibitor as well as NMDA receptor blocker and therefore may be useful in the treatment of AD.

Lautenschlager NT, Cox KL, Flicker L, et al. Effect of physical activity on cognitive function in older adults at risk for Alzheimer's Disease: a randomized trial. JAMA [Internet]. 2008 Sept 3 [cited 2009 Sept 17]; 300(9):1027-37

- This study, conducted in Australia, investigates the impact of regular physical activity on cognitive function. Specifically, they were interested in whether or not 24 weeks of home-based physical activity reduced the rates of cognitive decline in older adults at increased for, but not diagnosis of, dementia.

Nalivaeva NN, Risk LR, Belyaey ND and Turner AJ. Amyloid-degrading enzymes as therapeutic targets in Alzheimer's Disease. Current Alzheimer Research [Internet]. 2007 Dec 3 [cited 2009 Sept 16]; 5(2):212-24

- This review article examines novel enzymes responsible for amyloid plaque formation and degradation. It further describes ways in which these key enzymes may be used as a pharmacologic target in the treatment of AD.

For more information on Alzheimer's Disease, please refer to the following resources:

Alzheimer's Association
http://www.alz.org/index.asp

Alzheimer's Disease Education and Referral Center (ADEAR) from the National Institute on Aging
http://www.nia.nih.gov/alzheimers

Mayo Clinic (online)
http://www.mayoclinic.com/health/alzheimers-disease/DS00161

The Last "Dose"

"Thanksgiving dinners take eighteen hours to prepare. They are consumed in twelve minutes. Half-times take twelve minutes. This is not coincidence."
~Erma Bombeck

An electronic bulletin of drug and health-related news highlights, a service of …
Auburn University, Harrison School of Pharmacy, Drug Information Center
• Phone 334-844-4400 • Fax 334-844-8366 • http://www.pharmacy.auburn.edu/dilrc/dilrc.htm
Bernie R. Olin, Pharm.D., Director
Archived issues are available at: http://pharmacy.auburn.edu/dilrc/au_informed.htm