Memory Care Monthly

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Study Provides Further Evidence that The **MCI Screen** Accurately Detects Mild Cognitive Impairment

A recent study, the Hancock County Aging Study, found 23% of patients in a primary care population had cognitive impairment. However, two-thirds of those who were diagnosed as impaired had no outward symptoms or functional decline. The MCI Screen enabled the diagnosis of pre-symptomatic patients and identified impaired patients much more accurately than assessments that have traditionally been used by clinicians. This high level of accuracy is in line with the findings of a peer-review study published in the Proceedings of National Academy of Sciences (Shankle, W. R. et al, (2005), PNAS, 102(13), 4919-4924) verifying that the MCI Screen is 97.3% accurate in distinguishing between Mild Cognitive Impairment (MCI) and normal aging. The recent findings were presented on July 17, 2006 at the 10th International Conference on Alzheimer's disease and Related Disorders, presented by the National Alzheimer's Association held in Madrid, Spain.

The MCI Screen was more effective at identifying patients with memory impairment than the MMSE and the Clock Drawing Test

	Overall Accuracy	Sensitivity	Specificity
MCI Screen	97%	96%	99%
Mini Mental Status Exam	76%	72%	68%
The Clock Drawing Test	69%	52%	70%

New Guidelines for the Care of Patients with Dementia due to Alzheimer's

In order to guide clinicians with evidence and expert opinion regarding the care of patients with Alzheimer's disease, the American Association for Geriatric Psychiatry (AAGP) developed a position paper which was published in the July Issue of the *American Journal of Geriatric Psychiatry* and is available online at: http://www.aagponline.org/prof

The care model includes a series of therapeutic interventions, both pharmacologic and nonpharmacologic. The goals of treatment are to delay disease progression and functional decline, improve the quality of health and dignity for patients and their caregivers, control symptoms and provide comfort during all AD stages.

"We are clearly in a period where we should all be thinking of Alzheimer's as a condition we can treat, even though we do not have a cure yet," said task force chair Constantine Lyketsos, MD, MHS, from Johns Hopkins School of Medicine in Baltimore, MD in a news release. ❖

Mild Cognitive Impairment is the first clinical stage of Alzheimer's disease and often lasts approximately seven years before progressing to mild Alzheimer's. Currently, up to 95% of Alzheimer's patients are diagnosed when the disease has progressed to the moderate stage. Diagnosing and treating Alzheimer's disease in the mild cognitive impairment stage will have a tremendous impact on patients, caregivers and the health system. "In Alzheimer's disease, the most common cause of memory impairment, the longest clinical studies have shown a delay in disease progression greater than 50% when treatment is initiated early" says Dr. William Shankle, Chief Medical Officer of Medical Care Corporation. "This delay often means that a patient spends their last years living more independently at home as opposed to confined to a care facility. Likewise, a delay in loss of independence and function reduces caregiver burden and healthcare costs."

Dr. Douglas Trenkle, D.O., a board certified internist in Hancock County, Maine, assessed the memory of 240 patients aged 65 and older as part of their annual physical exam. Of the 240 patients, 183 were evaluated further as follows: each patient was assessed with the MCI Screen and two other widely used tests, the Mini Mental State Exam (MMSE), and the Clock Drawing Test (CDT). Additionally, the Functional Assessment Test (FAST) was used to establish the degree of functional capability in each person, from normal function to mild dementia. Patients with at least one abnormal result on any of the three assessments were further evaluated in accordance with published diagnostic guidelines which include blood and imaging tests.

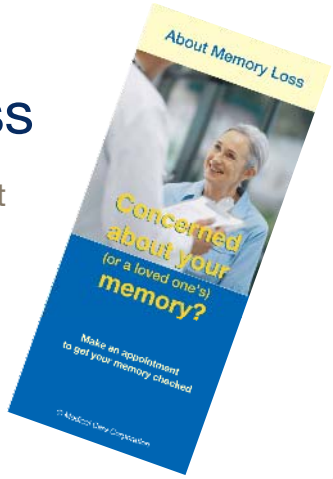
Post assessment and diagnosis, 22.4% of patients were determined to be impaired and had structural evidence of cerebrovascular disease, global or hippocampal atrophy, hydrocephalus or tumor, and had a history or laboratory findings supporting MRI findings. 63.4% of patients identified as impaired had no or minimal subjective symptomatology.

Applying a complex scoring mechanism, the MCI Screen was able to accurately detect 96% of the impaired patients even though the majority did not manifest functional impairment.

In comparison, the MMSE detected 72% of the cases and the CDT detected 57%. The MCI Screen also properly classified 99% of the cases of the unimpaired patients as normal. The MMSE classified 68% and the CDT classified 70% of those without impairments as normal. Accuracy for the MMSE was 76% and for the CDT 69%. The MCI Screen™ performed much better showing accuracy of 97%. ❖

Patient Brochures: About Memory Loss

Make sure your patients know that you now offer memory assessment services. We can send you complimentary copies of our educational patient brochure, "About Memory Loss". To request copies, please send an email to customerservice@mccare.com and include the address to where you would like the brochures mailed



The following two pages highlight research on dementia and Alzheimer's disease presented at the 10th International Conference on Alzheimer's disease and Related Disorders, organized by the National Alzheimer's Association and held in Madrid, Spain in July 2006

Impairment stage of Alzheimer's Disease and Treatment Mechanisms

The discovery by Mesulam et al that the cholinergic nervous system is affected at least as early as the MCI stage of AD. The key findings are that:

While the enzyme, choline acetyltransferase, is normal in MCI AD patients, there is an increase in the ratio of the enzymes which control cholinergic neuronal cell death (p75) and survival (trkA) in the MCI AD patients. This leads to increased degradation of NGF and increased amounts of proNGF in cholinergic neurons, both of which lead to progressive damage of cholinergic neurons. NGF delivery through gene expression vectors is currently entering phase III FDA trials and has been shown to significantly delay AD progression.

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There is a reduction in proBDNF and BDNF, both of which reduce cholinergic neuronal survival.

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The cell cycle is activated during MCI AD, which potentially increases new neuron formation. Leuprolide, a drug in phase III FDA trials, has the potential to stimulate neurogenesis and has so far been shown to slow AD progression.

Beta amyloid reduces NGF production to accelerate cholinergic neuronal death. In contrast, cholinergic neuronal stimulation increases cortical neuron regeneration and decreases beta amyloid production to slow AD progression. Phenserine is an M1 acetylcholinesterase inhibitor that increases cholinergic neuronal stimulation. It also reduces amyloid precuros protein production, which reduces beta amyloid production as well as increases neural stem cell differentiation. Exelon® also persistently increases cholinergic neuronal stimulation and helps explain why it delays AD progression during the dementia stage by approximately 54% for five or more years.

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Jones et al showed that long-term treatment with Aricept® reduces functional decline by 51% compared to 35% for placebo controls. Also, 40% of patients discontinued on Aricept® showed significant functional decline and needed to be restarted. The effect of Aricept® lasted for the full three years of the study.

Immunotherapy of AD

Immunotherapy of AD via passive immunization with anti-beta amyloid antibodies was shown to initially increase the rate of hippocampal tissue loss during the first year, but then it slowed the rate of tissue loss compared to cholinesterase inhibitor-treated controls over years two and three. The explanation for this is that during the first year, a large amount of beta amyloid was being removed from the cortex, which actually caused greater brain shrinkage than the control group. However, in years two and three, after most of the beta amyloid had been removed, the rate of brain shrinkage was less than that of the control group. Patients cognition and functionally declined 50% slower than that of the control group. Further confirmation of a positive effect of removing beta amyloid occurred in several patients treated with the Elan vaccine who died and were autopsied. Their brains showed massive reduction of the beta amyloid load in their brain. ❖

IDEAL (Investigation of transDermal Exelon in Alzheimer's Disease)

A 24-week, randomized, double-blind, placebo-controlled study of Exelon® once-daily patches vs. twice-daily capsules in 1195 patients with moderate AD were, for the first time, presented at the ICAD.

Study Group: These patients aged 50-85 years, with probable AD and MMSE scores 10-20, were randomized to one of four treatment groups: a once-daily10 cm^2 patch, a once-daily 20 cm^2, a 6 mg twice-daily capsule, or placebo. Efficacy was assessed at week 16 and 24 using ADAS-cog (cognitive assessment), ADCS-CGIC (global functioning assessment), and also the secondary efficacy parameters were used to assess other domains including attention, ADL, neuropsychiatric symptoms and patient preference.

Efficacy Measure: The study found that, compared to placebo, oral and transdermal formula provided significant improvements over 24 weeks assessed by ADAS-Cog and ADCS-CGIC. Changes from baseline measured by MMSE and ADCS-ADL were also significant in oral and transdermal formula compared to placebo. On the ADAS-Cog, effects were seen earliest, and tended to be greatest in magnitude, in the 20 cm^2 patch group although efficacy was similar across the 10 and 20 cm^2 patch and capsule groups on other measures.

Side Effect: The most common adverse events were nausea and vomiting. However, rates of nausea and vomiting were about 3 times lower with the 10 cm^2 patch (7.2 % and 6.2 %, respectively) and with the capsule (23.1% and 17.0%, respectively). In 20 cm^2 patch group, 21.1 % of patients reported nausea and 18.8 % reported vomiting. Incidences of these adverse events in placebo were 5.0 % and 3.3 % for nausea and vomiting, respectively. Other common side effects were skin irritation (e.g. erythema). However, this was absent or only slight or mild in most of the patients, and no unexpected safety issues were observed.

Patient and Caregiver Preference: Previous studies in other indications by Audet et al have demonstrated that patch formulations are a more preferable option for patients than pills, and can results in greater patient compliance. In the IDEAL study, caregivers' preference was assessed, and more than 70 % of them preferred the patch over the capsule formulation. At each follow-up assessment, the patch was significantly preferred to capsules for ease to follow schedule and ease of administration. Also caregiver indicated greater satisfaction over all, greater satisfaction with administration, and less interference with daily life with the patch compared with the capsule formulation.

Current therapies approved for AD are all orally administered, and could potentially cause difficulties in compliance. The improved patient compliance and longer duration of action associated with patch formulations provide a therapeutic rationale to predict additional benefits in AD patients. ❖

Reduction of Tau Hyperphosphorylation with Memantine

With regard to memantine, Iqbal et al showed that memantine reduces hyperphosphorylation of tau proteins at brain levels that are easily achieved clinically. Tau hyperphosphorylation leads to the neurofibrillary tangles of AD pathology and was shown to produce cognitive impairment. ❖

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