Moving Past Conventional Wisdom in AD Therapy

Several new advances in AD treatment provide evidence that researchers are looking beyond the tried-and-true in hopes of making progress on roads less traveled.

• Immunomodulatory therapy for Alzheimer's shows promise, says Baxter International, based on the results of its phase II study of gammagard IVIg in AD. The company has planned a phase III study. Twenty-four patients—eight on the newer liquid form of the drug, eight who received the older form and eight on placebo—are involved in the randomized trial. The endpoint of the study is a review of cognitive function and global function.

• That treatment with statins in some epidemiologic studies has found an association with a reduced risk in AD has been looked at before, but a study published in the August 28th issue of *Neurology* sought to investigate "whether antecedent statin exposure is associated with neuritic plaque (NP) or neurofibrillary tangle (NFT) burden in a population-based sample of human subjects." The authors concluded there was a connection linking antecedent statin use and neurofibrillary tangle burden at autopsy. Researchers executed brain autopsies on 110 subjects between the ages of 65 and 79 who were cognitively normal at the time of their enrollment in the Adult Changes in Thought Study. Though caution is certainly warranted, as other touted studies have found little or no benefit of statins on AD.

They controlled for age at death, gender, cognitive function at entry of study, brain weight, and presence of cerebral microvascular lesions, and found the odds ratio for each unit increase in Braak NFT stage in statin users vs nonusers was 0.44 (95% CI: 0.20 to 0.95). "The OR for each unit increase in Consortium to Establish a Registry for Alzheimer's Disease (CERAD) staging of NPs did not deviate significantly from unity (OR 0.69; 95% CI: 0.32 to 1.52)." Although "the risk for typical AD pathology (Braak stage IV and CERAD rating moderate) was reduced in statin users (OR 0.20; 95% CI: 0.05 to 0.86)."

• The nose may be the new frontier in treating Alzheimer's disease, according to new research from Tel Aviv University. Sending filamentous bacteriophages through nasal passages allows them to lock onto plaque associated with AD, dissolving it, says Professor Beka Solomon, presenting her research in Canada at a meeting of the American Society of Microbiology. In the study, mice were administered the phage and Prof. Solomon noted that those which had shown signs of AD symptoms had their sense of smell return and displayed improvement in memory. Following 12 months of treatment, they had 80 percent fewer plaques than mice that received no treatment.

• A new study funded by the National Institute on Aging is testing the hypothesis that daily use of DHA (docosahexaenoic acid) slows the progression of cognitive and functional decline over 18 months in mild to moderate Alzheimer's. A preclinical study published in *Journal of Neuroscience* this past April found that the drug, an omega-3 fatty acid, improved cognitive function and slowed cognitive decline. The study intends to enroll about 400 participants with mild to moderate AD, who'll be randomized to either 2000mg of DHA or placebo, and can continue to their existing Alzheimer's regimen.

• A new study says the rivastigmine transdermal patch has displayed a "favorable" safety profile after one year of treatment. Presented at the 2007 European Federation of Neurological Society meeting, the study demonstrated that once-daily Exelon patch showed comparable efficacy to the highest doses of rivastigmine capsules (12mg/day) and gave considerable benefits to patients in regard to memory, cognition and activities of daily living. The target dose of the Exelon patch (9.5 mg/24 hours) was generally well tolerated and had three times fewer reports of nausea and vomiting. The findings are a result of the 28-week, open-label extension phase of the IDEAL trial. **PN**

SHORTTAKES

■ **Envisioning Successful Recovery.** Brain activity may be increased in stroke and traumatic brain injury patients who go through Vision Restoration Therapy, according to a new study published online August 14th in *Neurorehabilitation and Neuronal Repair*. Researchers reviewed the fMRI scans of six patients between the ages of 35 and 77 who underwent the rehabilitative treatment—which helps patients recover lost vision—and had vision loss on the same side of both eyes triggered by stroke or traumatic brain injury. Increased activity in visual processing regions of the brain was seen in the fMRI scans after patients learned to detect stimuli in the area between seeing and non-seeing fields. One month after treatment began, the enhanced activity was identified, which suggested that the brain responded fittingly. Patients performed the therapy on a daily basis at home on a computer device.

■ **Antithrombotic Therapy Linked to GI Bleeds.** The risk of gastrointestinal bleeding may be much higher when antithrombotic therapy is combined with ASA or NSAIDs. A population-based, retrospective, case-control study published online August 14th in the *Canadian Medical Association Journal* found a four-to six-fold increased risk for GI bleeds among patients who had taken warfarin or clopidogrel with ASA or NSAIDs. Researchers found 4028 patients presenting with their first diagnosis of GI bleeding and were over the age of 18 from 400 general

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The Next Internet Sensation: You?

The popular social-networking web sites MySpace and Facebook allow users to post information about themselves, such as their favorites movies, interests and activities. Now, due to a recent decision by a federal judge in Washington, DC, information about you may also be released to the public. But instead of sharing that *Field of Dreams* is your favorite movie, your profile might include how many times you perform Botox injections and when you order MRI and CT scans, among other things.

A lawsuit filed by Consumers' Checkbook—a non-profit group that ranks everything from window installers to cell phone service, for a fee—will now force HHS to release specific data about physicians from the Medicare claims database, a number more than 700,000 strong. The ruling applies to DC, Illinois, Maryland, Virginia and Washington state, but the group has filed a Freedom of Information Act request for the rest of the country. "Consumers, physicians and the Medicare program itself will benefit greatly when these data are used in measures of physician experience, quality and efficiency," says Robert Krughoff, President of Consumers' Checkbook, in a press release.

"It is unclear what information will be released," says Marc Nuwer, MD, Professor of Neurology at UCLA School of Medicine. "I sort of understood it to be the Medicare volume and payments for various CPT codes, presented as a list by physician." And given programs like the Physician Quality Reporting Index and doctor rankings by health plans like Aetna and Cigna, public access to physician quality and experience assessments is being explored more and more.

The value of the database had been restricted due to a decades-old policy that protected the information of doctors. But in his written opinion, US District Court Judge Emmet G. Sullivan said only part of physicians' business transactions are at risk of disclosure, "not intimate facts about their personal lives. [D]isclosure of the physician information is not 'clearly unwarranted' in the light of the important public interests at stake."

While one hope is that the information will tell consumers how many times a physician has performed a procedure—likely translating to how "good" a doctor is, in their minds—some feel breaking down and interpreting the information will be too difficult for the general public. "I've used those databases myself for other purposes," Dr. Nuwer says. "It would seem to me to be difficult for a patient to understand what that means. Someone would have to substantially enhance the data to make it meaningful."

This is where the services of Consumers' Checkbook would likely come into play. The group typically charges between $10 to $15 for their rankings and reports, but says it intends to give the Medicare data away free of charge.

Speaking in general about the concept—rather that about Consumers' services per se—Dr. Nuwer says he suspects "that the public data would be very hard to use, open to many different interpretations, easy to twist into incorrect statements." Several factors cause numerous interpretations of the same data. Billing codes can overlap, different offices can use them differently and seeing a drastically higher-than-normal number of patient deaths can cause potential patients to run away from certain doctors, not taking into account the physician might only see the sickest of patients.

The lawsuit will not reveal any information on patients. HHS is unlikely to appeal the ruling. **PN**

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practices included in the United Kingdom General Practice Research Database between 2000 and 2005. They were then matched with 40,171 controls from the same database.

■ **Expanding the AED Options.** An AED with a novel mechanism of action could be headed to market if clinical trials support FDA approval. Retigabine, a potassium channel opener used in patients with refractory partial-onset seizures taking one to three concomitant AED treatments, is currently being studied in the Retigabine Efficacy and Safety Trials for Partial Onset Epilepsy (RESTORE) and will soon enter phase III testing, according to Valeant Pharmaceuticals. The company says 306 patients have enrolled at 49 sites; it expects completion in the first quarter of 2008. The primary endpoint of RESTORE1 is a change in total partial seizure frequency per four weeks from baseline to the double-blind period. Another trial, RESTORE2, will enroll 510 patients at 72 sites.

■ **Room For One More?** Since the first day of med school, conventional neurological wisdom has held that the loss of dopamine triggered the onset of symptoms of Parkinson's disease. Now, research published in the August 21st edition of *Proceedings of the National Academy of Sciences* indicates there may be a link between the loss of both dopamine and norepinephrine and the delayed onset of PD symptoms. The authors gave healthy, one-year-old mice the neurotoxin MPTP in a dose that would eliminate 80 percent of dopamine but no motor impairments in the mice was noticed. However, when mice unable to synthesize norepinephrine and had trouble creating dopamine properly were tested, they saw symptoms of PD (resting tremor, hunched posture, deficits in coordinated movement). Researchers believe these results show that a normal quantity of dopamine is not adequate for standard motor function and that norepinephrine must also be present for suitable release of dopamine.