



RA News Relevant to Neurologists

Neurologists often play a role in the diagnosis, management, and long-term monitoring of patients with rheumatoid arthritis. With relatively new treatments available and more emerging, it's important to keep up to date on the latest findings. Here are some highlights from the American College of Rheumatology/Association of Rheumatology Health Professionals annual meeting:

- Anti-TNF therapies used to treat rheumatoid arthritis do not seem to cause cancer. Researchers in Spain recently looked to BIOBADASER, a drug registry established in 2001 for the active long-term follow-up of the safety of biological therapies in rheumatology patients, which included 4,529 patients with RA who had been treated with TNF antagonists. Researchers looked at this group of patients, and a control group of patients with RA not included in the BIOBADASER registry that were followed from 1999 to 2005, to estimate cancer rates in patients with RA who were treated with TNF antagonists versus controls.

After a total follow up of 14,001 person years, researchers found 29 cases of cancer in the control group and 70 in the TNF-treated group. After adjusting for variables, they found that the incidence of developing cancer in the TNF group was very close to that of the non-TNF treated control group (0.92).

- Mouth exams aren't typical of the average neurology consult, but RA patients should be counseled to monitor oral health and have regular dental exams. One study looked for periodontal disease in 153 patients ages 45 to 84 who had RA for 11 years, on average. Investigators found periodontal disease was significantly linked with a patient's RA disease activity score and with rheumatoid nodules. "These findings, along with prior studies and our additional preliminary data showing a high prevalence of moderate to severe periodontal disease in RA patients based on comprehensive oral examinations, strongly suggest an association between these two inflammatory diseases,"

author Clifton O. Bingham, MD says in a news release.

- Etanercept and methotrexate appear safe and effective for long-term, continuous treatment of juvenile arthritis. Researchers followed 204 patients for three years with 66 taking methotrexate alone, 333 taking etanercept alone, and 105 taking a combination of the two drugs. Etanercept was administered as either a 0.4mg/kg injection twice weekly or 0.8mg/kg weekly, and methotrexate was given at a dose greater than or equal to 10mg/m² once a week. Researchers concluded that, "These data suggest that etanercept, alone or in combination with methotrexate, is safe as long-term continuous therapy for the treatment of juvenile rheumatoid arthritis." **PN**

Toward Diagnostic Imaging for AD?

Use of brain imaging to identify early Alzheimer's disease may be nearing clinical reality, with researchers preparing to launch phase 3 diagnostic imaging studies for new imaging biomarkers. Investigational agents, designed to show amyloid on PET scans, could potentially be used to diagnose AD, rule out AD, or monitor response to therapy. The agents, developed in collaboration by Bayer Healthcare, GE Healthcare, and Avid Radiopharmaceuticals, have a half-life of two-hours.

Representatives from the three companies met with an FDA advisory panel last month, seeking guidance on design of the phase 3 investigations. The panel advised the developers that trials must include post-mortem examination of the brains of AD patients. **PN**

SHORT TAKES

■ **Inflammatory Research.** Structural and neurochemical features of schizophrenia are present before the disease develops. So what process is the straw that breaks the back between high-risk states and the development of schizophrenia? New research in *Biological Psychiatry* (Nov. 1) says one candi-

date is cerebral inflammation. PET imaging found evidence of a brain inflammatory state that could be associated with the development of schizophrenia. For the study, 10 patients with recent-onset schizophrenia and 10 age-matched healthy control subjects were included and a fully quantitative (R)-[(11)C]PK11195 PET scan was performed on all subjects, including arterial sampling to generate a

metabolite-corrected input curve.

Compared with control subjects, binding potential of (R)-[(11)C]PK11195 in total gray matter was increased in patients with schizophrenia. There were no differences in other PET parameters. The authors also noted that "activated microglia are present in schizophrenia patients within the first 5 years of disease onset." →

Banning Physician Gifts and the Effects

Doctors in the Copper State may not be able to take so much as a penny as a gift from the pharmaceutical industry if the Wisconsin Medical Society's Board of Directors gets its way. The Board is trying to squash conflict of interests outright by banning all gifts. While some state legislatures, medical boards, and companies are moving to disclose physician payments, the Wisconsin Medical Society's Board passed regulations that will ban *all* gifts.

The Relationship of the Profession to the Health Product Industry policy reads in part: "Physicians shall accept

no gifts from any provider of products that they prescribe to their patients such as personal items, office supplies, food, travel and time costs, or payment for participation in on-line CME. A com-

The policy references a *Journal of the American Medical Association* article (2006;295:429-433) that details the impact of gifts on trust in the physician-patient relationship and proposes "a poli-

cy under which academic medical centers would take the lead in eliminating the conflicts of interest that still characterize the relationship between physicians and the health care industry." With that article as a guide, the Wisconsin policy also provides exam-

ples of ethical behavior in the areas of handling drug samples and physicians serving on formulary committees or speaker bureaus, and describes how the

Only 56 percent of physicians say they are willing to meet with drug sales reps, and only 24 percent want to spend more than two minutes with one.



SHORT TAKES

■ **Rodent Reversal.** It was the mouse that removed the thorn from the lion's paw in the ancient children's fable and it could be a study on mice that sheds light on a new treatment for Alzheimer's disease. Researchers found that if valproic acid is used as a treatment in the early stages of a mouse model of AD that memory deficit is reversed. They say in the *Journal of Experimental Medicine* (Oct. 27, 2008) that the common epilepsy drug works by inhibiting the activity of an enzyme that produces beta amyloid. The drug further prevented brain cell death and axon damage and improved performance in memory tests. A small human clinical trial is currently taking place, and study authors expect results to be available in the next year.

■ **Midwest Winners.** Patients in the Midwestern US taking anti-seizure medications prescribed by a neurologist maintained their therapy 16 percent longer than the national average of 142 days, according to data from SDI, a pharmaceutical and healthcare analysis company. The data, taken from July 2007 through July 2008, found that in general, patients in the Midwest maintain their anti-seizure medication approximately four percent longer than the national average. Most important, the length of therapy is extended when a neurologist initiates the prescription versus another physician.

■ **The Incredible Shrinking Brain.** The more alcohol a person drinks, the smaller their wallet gets. Unfortunately, that might not be the bad news. According to a study in *Archives of Neurology* (65(10):1363-7) the

more booze bar patrons put back, the smaller his or her brain volume. Researchers studied 1,839 adults, who had an average age of 60, and were part of the Framingham Offspring Study, which began in 1971. Participants underwent MRI and health examinations, and researchers concluded "there was a significant negative linear relationship between alcohol consumption and total cerebral volume." The study found that though men were more likely to drink alcohol, the connection between drinking and brain volume was stronger in women.

■ **Vit D in PD and AD.** Parkinson's disease patients are more likely to have vitamin D deficiency than healthy adults of the same age or patients with Alzheimer's disease, according to *Archives of Neurology* (65(10):1348-52). Study authors compared vitamin D levels of 100 patients with PD to

of Drug Reps on Doctors

industry can still support needed CME offerings.

The move is part of a national push for greater transparency. Recently, Eli Lilly made news when it announced it would become the first drug company to disclose physician payments of \$500 or more to the public. Congress has also advocated stronger regulations on physician payment disclosure.

But one analysis says that doctors across the US are already skeptical of those who provide many of the gifts under scrutiny in Wisconsin. Only 56 percent of physicians say they are willing to meet with drug sales representatives, and only 24 percent want to spend more than two minutes with one, according to analysis by Oliver Wyman, a management consulting firm. Eighty-six percent of physicians think the information sales representatives share is biased and doesn't tell the whole story

Areas of Scrutiny for Conflicts of Interest

The 2006 JAMA article called for "Elimination or modification of common practices related to":

- Small gifts
- Pharmaceutical samples
- Continuing medical education
- Funds for physician travel
- Speakers bureaus
- Ghostwriting
- Consulting and research contracts

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of the product, at best.

"Physicians don't like the hard sell," says Jim Hall, an Oliver Wyman spokesperson. "They are looking for unbiased data that explains efficacy, outcomes, and patient value." **PN**

SHORT TAKES

vitamin D levels of 97 AD patients and 99 healthy individuals matched for age, gender, race, genotype and geographic location. "Significantly more patients with Parkinson's disease (55 percent) had insufficient vitamin D than did controls (36 percent) or patients with Alzheimer's disease (41 percent)," the authors write.

"These findings support the previously suggested need for further studies to assess what contribution a low 25(OH)D concentration adds to the risk of developing Parkinson's disease (vs. other neurodegenerative disorders) and to determine whether correction of vitamin D insufficiency and deficiency will improve motor or non-motor symptoms in Parkinson's disease," the authors conclude.

■ **Stimulating Headaches.** Using a nerve stimulating bion to disable headache disorders improved pain symptoms by 80 to 95 percent, according to a study published in *Lancet Neurology* (7(11):1001-12). The rechargeable battery-powered electrode, similar in size to a matchstick, was implanted near the occipital nerve in the back of the neck in six patients aged 37 to 64 with hemicrania continua. Patients received continuous stimulation for first three months, had it switched off in the fourth month, and resumed stimulation again in month five, the fourth month effectively becoming a de facto placebo.

Researchers discovered that within a range of six to 21 months after implanting the devices, five of the six patients reported "sufficient" benefit to recommend the device to other people with hemicrania continua. ■



■ **On Hold.** The FDA said it was unable to take action by the scheduled Prescription Drug User Fee Act action date of Oct. 18 on the NDA for milnacipran, a selective serotonin and norepinephrine reuptake inhibitor for the treatment of fibromyalgia. The agency didn't request any more information from the drug's maker but posed a clinical question related to the NDA. The makers plan for a first quarter 2009 product launch meeting.

■ **Stalevo x 2.** There are two more dosage-strength formulations of Stalevo (Novartis Pharmaceuticals) available to manage PD patients. The FDA approved Stalevo 75 (18.75mg carbidopa, 75mg levodopa, 200mg entacapone) and Stalevo 125 tablets (31.25mg carbidopa, 125mg levodopa, 200mg entacapone), now available in pharmacies. Stalevo is indicated for people with PD who experience end-of-dose "wearing off."

■ **Vimpat Approved.** Vimpat (lacosamide, UCB) received the FDA nod for use as an add-on therapy for treatment of partial-onset seizures in people with epilepsy age 17 and older. In preclinical studies, Vimpat's novel mechanism of action was shown to involve prolonging the resting state of the sodium channel, a different action compared with current sodium channel blockers. Lacosamide has also been shown to bind to the collapsin response mediator protein-2 (CRMP-2), which affects nerve differentiation and growth.

Clinical trials with approximately 1,300 people with epilepsy age 16 and older who had uncontrolled partial-onset seizures found that treatment reduced the number of seizures by half with significantly greater reductions in median seizure frequency versus placebo. The most common AEs reported included diplopia, headache, dizziness, and nausea. Dosing starts at 50mg BID and may be increased to 200-400mg/d (recommended therapeutic dosing) in two divided doses. Vimpat will be available as oral tablets and as an IV. ■