“Each month you’ll find ideas that take to heart the Apple Computer ad campaign motto, ‘think different.’” So wrote Jack Persico, founding editor-in-chief of *Practical Neurology* magazine in its inaugural edition in January 2002. Back then, Apple was known for its computers, tissue plasminogen activator was a novel idea, and print magazines were a primary source of information.

Indeed, much has changed in the field of neurology and in the larger spectrum of healthcare since then—electronic medical records are now commonplace in medical centers and practices nationwide, landmark legislation has altered the healthcare landscape, and ever refined standards of reimbursement and certification are changing the physician’s profession.

Yet, as we look back on 15 years in publication and consider the many developments and new ideas we’ve covered with fresh insights from leading voices in the field, the common theme that’s emerged amid so much volatility in the healthcare market is innovation—in technology, research, drug development, and patient care.

Here at *Practical Neurology* we plan to keep on “thinking differently,” as we bring you coverage of the newest advances in the field. Next year we are launching several new regular departments, from disease-specific resource centers to regular coverage of the latest in teleneurology. In addition to the quality content you’ve come to expect in the print edition, we will expand our digital presence through new video programs, more coverage of key meetings, and the launch of a brand-new user-friendly website in 2017.

As the field evolves, you can count on *Practical Neurology* to bring you fresh and nuanced perspective on all matters of concern to the practice of neurology. We look forward to continuing the serve you.

—Ted Pigeon, Editor-in-Chief

**WEB EXCLUSIVE:**

Visit practicalneurology.com for brief commentaries from members of the founding editorial team of *Practical Neurology*, including Jack Persico and Chief Medical Editor Stephen Gollomp, MD.
Lilly’s Solanezumab Fails in Phase 3 Trial

In a blow to the emerging class of amyloid-based agents for Alzheimer’s disease, results from the recent EXPEDITION3 trial showed that Eli Lilly’s experimental agent solanezumab did not meet its primary endpoint in people with mild dementia due to Alzheimer’s disease (AD). Researchers were expecting to see patients treated with the agent experience a slowing in cognitive decline as measured by the ADAS-Cog14 (Alzheimer’s Disease Assessment Scale-Cognitive subscale), but the results did not yield a statistically significant decline. Lilly has since suspended plans for regulatory submission, while next steps for the development program have not been decided.

Oral Bacteria Linked to Migraine

Oral bacteria that convert nitrates into nitric oxide in the blood may be the key to understanding the cause of migraines, according to newly published findings. In a study published in *mSystems* from the American Society for Microbiology (1(5):e00105-16.), migraine sufferers were found to have higher levels of nitrate, nitrite, and nitric oxide reductase genes. Researchers used high-throughput sequencing technologies to evaluated oral cavity and fecal samples and found “small but significant increases” in nitrate, nitrite, and nitric oxide reductase genes in stool samples collected from migraineurs, while in the oral samples these same genes were more abundant. “Future research should focus on further characterizing the connection between oral bacterial nitrate, nitrite, and nitric oxide reducers and migraines,” the authors wrote.

New MRI Labeling Approved for St. Jude Medical’s SCS System

The FDA has approved new labeling for full-body magnetic resonance imaging (MRI) for St. Jude Medical’s Proclaim Elite Spinal Cord Stimulation (SCS) System. The new labeling ensures patients in need of future full-body MRIs can have access to the recharge-free Proclaim Elite SCS System and the company’s proprietary BurstDR stimulation technology, according to the company. Full-body MRI compatibility is the second major upgrade to the Proclaim Elite SCS system following the recent approval of BurstDR stimulation. Current and future patients who get the Proclaim Elite SCS system will now have access to both full-body MRI scans within approved parameters and BurstDR stimulation. St. Jude Medical designed the Proclaim Elite SCS system to offer patients future approved upgrades through software updates without the need to surgically replace their device.

Tramiprosate Shows Gene-Dose Effect in Alzheimer’s Patients with APOE4

New phase 3 findings suggest that the investigational amyloid-targeted agent tramiprosate may be particularly effective for patients with 4 alleles of apolipoprotein E (APOE4), a genetic risk factor in mild to moderate Alzheimer’s disease (AD). In a study published in *The Journal of the Prevention of Alzheimer’s Disease* (2016; 3(4): 219-228), investigators evaluated patient subgroups based on the number of APOE4 alleles. The results showed a gene-dose effect at the high dose of tramiprosate (150 mg, twice daily), with patients with two APOE4 alleles (APOE4/4 homozygotes) showing the largest clinical benefit, those with one APOE4 allele (APOE4 heterozygotes) showing an intermediate benefit, an APOE4 non-carriers showed no benefit from tramiprosate. The results represent the first evidence from a large clinical trial to associate efficacy of an amyloid-targeted agent with APOE4 status in AD patients.

The study was sponsored by Alzheon, which is developing ALZ-801, an optimized oral prodrug of tramiprosate. Based on the analyses, the company has refined the design of its pivotal phase 3 clinical trial to evaluate ALZ-801 as a potential disease-modifying agent in symptomatic AD patients who are APOE4/4 homozygotes.

AMA Honors Omalu, Adopts Policies to Further CTE Research

The American Medical Association (AMA) has recently adopted new policies urging further research into the detection, causes, and prevention of head injuries. In particular, the policies encourage efforts to develop diagnostic tools as well as to understand preventive measures that can protect against chronic traumatic encephalopathy (CTE).

During the opening session of its recent Interim Meeting, the AMA honored Bennet I. Omalu, MD, MBA, M.P.H., with
Saliva Test May Detect Alzheimer’s Disease

A new saliva test developed by Aurin Biotech could serve as a diagnostic marker for Alzheimer’s disease, according to new findings published in The Journal of Alzheimer’s Disease (October 24, 2016). The test is based on measuring the concentration of amyloid beta protein 42 (Abeta42) secreted in saliva. Abeta42 is the material which accumulates in the brain of Alzheimer disease cases and causes neuroinflammation which kills brain neurons. In the study, researchers found that those with Alzheimer’s disease secreted more than double the levels of Abeta42 than controls. Additionally, individuals at elevated risk of developing AD secreted levels comparable to the AD cases. “The number of cases studied is small, but our results are so remarkable, we felt they should be made widely available,” explained Dr. Pat McGeer, President and CEO of Aurin Biotech, in a release. “If individuals know they are destined to develop Alzheimer disease, they can initiate preventive measures. These include taking over-the-counter non-steroidal anti-inflammatory drugs such as ibuprofen, drinking coffee, and sticking to a Mediterranean diet.”

Genetic Mutation Tied to Risk of Early Parkinson’s Disease

Aging appears to alter how genetic factors contribute to the development of Parkinson’s disease, according to new research that has identified a gene that may increase risk of early onset Parkinson’s disease. Investigating the differences between functional polymorphisms at RS11158026 coding for guanosine triphosphate cyclohydrolase-1 (GCH1), researchers found that T allele carriers showed higher PD risk and earlier age of onset by five years compared to age-matched controls. (Neurobiol Aging. 2016 Oct 13;50:39-46). Carriers also had lower striatal dopamine reuptake transporter uptake, increased cerebrospinal fluid, as well as worse motor function, anxiety, and executive function. Of note,
these effects were only in younger T carriers (younger than 50 years), where aging quells the effects of these genetic factors, the researchers found. They suggested that future studies investigate how aging modifies genotypes’ contributions on PD risk and sequelae.

**Adjunctive Treatment with Lyrica Found to Reduce Seizure Frequency in Pediatric Epilepsy**

New phase 3 results show that Lyrica (pregabalin, Pfizer) Capsules CV is an effective adjunctive therapy for patients with epilepsy between the ages of four and 16 years of age. Specifically, the results showed that adjunctive treatment with Lyrica 10 mg/kg/day resulted in a statistically significant reduction in seizure frequency versus placebo at 12 weeks. Patients receive Lyrica at a dosage of 2.4 mg/kg/day also experiences a numerical reduction in seizure frequency, however this was not statistically significant. Of note, the safety profile observed in the study was consistent with previous findings, with the most common adverse events being somnolence, weight increase, increased appetite, and pyrexia.

The study was part of the Lyrica Pediatric Epilepsy Program to evaluate Lyrica as an adjunctive therapy for the treatment of pediatric epilepsy. Three studies have been completed in the program and three are actively enrolling.

**More Headlines from NeurologyWire**

**Phase 1 Data Show Rapid Absorption of Intranasal Midazolam in Pediatric Patients with Epilepsy**

New Phase 1 data show that intranasal midazolam spray (USL261, Upsher-Smith) in pediatric participants with epilepsy is rapidly absorbed and with no dose-dependent differences in maximum plasma concentration. USL261 is being developed for the rescue treatment of seizures in patients who require control of intermittent bouts of increased seizure activity, such as seizure clusters or acute repetitive seizures. It is intended for intranasal delivery and without active inhalation by the patient.

In a presentation at the Child Neurology Society (CNS) annual meeting in Vancouver earlier this year, researchers shared findings demonstrating that USL261, administered as single doses of 1.25 mg, 2.5 mg or 5 mg, were similar in mean maximum observed plasma concentration and time to peak plasma concentration, roughly 35 ng/mL and 15 minutes, respectively. They also observed that area under the concentration time curve (AUC) values were higher in the 5 mg group versus the 1.25 or 2.5 mg groups. The most common TEAEs were somnolence and product taste abnormal.

The findings support the continued development of USL261 in this population, according to the investigators.

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