We Are All Headache Specialists

Erenumab approval heralds a new era in headache medicine.

By Peter McAllister, MD

Welcome to the inaugural Headache Horizons column. Our mission is to provide timely, lively, and—in keeping with this journal's title—practical articles on all things headache. It is an exciting time to launch Headache Horizons, as we stand on the cusp of an explosion of acute and preventive treatment options for headache that are based on an increasingly clear picture of pain-processing pathophysiology.

Headache Medicine, a Relatively New Subspecialty

Although care of patients with headache in a neurology office is commonplace, headache medicine is a relatively new subspecialty. In 1998 the American Academy of Neurology (AAN) convened a panel to study the idea of subspecialty certification, which led to the formation of the nonprofit United Council for Neurological Subspecialties (UCNS), endorsed by key stakeholders including the American Neurological Association, Child Neurology Society, and the Association of University Professors of Neurology.[1] There are now 9 UCNS-recognized subspecialties (Table). The first UCNS certification examination for headache medicine was offered in 2006, and of the 106 physicians who took the test, 105 passed. There are now 484 board-certified headache specialists and 36 accredited headache fellowship training programs. Regional disparities are significant; for example, there are >30 certified headache specialists in California, Texas, New York, and New Mexico, whereas there are none in Alaska, North Dakota, and Montana.[2]

There are nearly 38 million people with migraine in the US, and although migraine is a substantial subset, it is still only a subset of all headaches experienced. If all patients with migraine were cared for by a UCNS board-certified headache specialist, each would see approximately 78,000 patients per year (215 patients/day, 365 days of the year). Talk about physician burnout!

TABLE. UNITED COUNCIL FOR NEUROLOGIC SUBSPECIALTIES

Subspecialty	Year Begun
Autonomic disorders	2009
Behavioral neurology	2006
Clinical neuromuscular pathology	2015
Geriatric neurology	2009
Headache medicine	2006
Neural repair and rehabilitation	2012
Neuroimaging	2008
Neuro-oncology	2008
Neurocritical care	2007

We All Treat Patients With Headache

The impossibility of these numbers reinforces an obvious point: all neurologists (and interested internists, family practice physicians, psychiatrists, nurse practitioners, and physician assistants) need to consider themselves headache doctors, because the majority of patients with headache will never see the inside of a UCNS board-certifed headache specialist's office. Referrals to board-certified headache specialists should be reserved for patients who fail front-line (primary care) treatment and secondary treatment by general neurologists.

The Old Era

Unfortunately, for many neurologists, headache medicine is the red-headed stepchild of our field. Neglected in medical school and residency training, headache medicine is too often considered inferior to so-called real or hardcore neurology that encompasses (and perhaps places an inordinate emphasis on) disorders considered more serious (eg, stroke, myasthenia gravis, movement disorders, or amyotrophic lateral sclerosis). In contrast to these, primary headache disorders are still too often viewed through a jaundiced lens that

sees them as little more than inconveniences, trivialities, or uncomfortable neuroses largely confined to a certain population composed primarily of anxious women. Although there are 38, 95, and 633 persons with migraine for every person with Parkinson's, multiple sclerosis, and myasthenia gravis respectively, headache medicine, much like the late Rodney Dangerfield, "don't get no respect."

Migraine is 1 of the top 5 most disabling medical conditions,[3] and cluster headache is the number 1 most painful medical condition (trigeminal neuralgia, neuropathy, and complex regional pain syndrome are also among the top 10.[4] Headache is the most common symptom of concussion and traumatic brain injury, and chronic posttraumatic headache affects more than 40% of veterans of the Afghanistan and Iraq conflicts. Unfortunately, although this shows that diagnosis and care of persons with headache should be paramount in any neurology practice, we have ample data that headache disorders are both underdiagnosed and undertreated.[5]

A generation ago, the release of sumatriptan heralded an exciting—perhaps short-lived—paradigm shift for migraine pathophysiology. Having a first specific acute treatment for migraine lent a welcome air of scientific validity and reinforced that migraine was every bit as biological as any other disorder neurologists treat. As triptans became commonplace, however, the buzz of excitement and enthusiasm for headache medicine diminished. Despite this, research continued, and slowly, headache began to come out of the proverbial black box, as we learned more and more about nociceptive pathways, neuropeptides, allodynia, central sensitization, and the epidemiology and burden of disease.[6]

A New Era

Now, the dawn of the calcitonin gene-related peptide (CGRP) era has arrived. Years from now, medical historians may very well divide headache medicine into pre- and post-May 17th, 2017, much like we divide geopolitical history between pre- and post-September 11, 2001. Because on this monumental day, May 17th, 2018, the Food and Drug Administration (FDA) approved erenumab (Aimovig; Novartis, East Hanover, NJ and Amgen, Thousand Oaks, CA) a CGRP receptor-blocking monoclonal antibody, for the preventive treatment of migraine in adults.[6] Erenumab is available in a 70-mg EpiPen-like device for monthly subcutaneous injections of either 70 mg or 140 mg. The cost of either dose before insurance is $575 a month.

This new era of CGRP receptor- and ligand-blocking monoclonal antibodies appears to be nothing short of game-changing. Referring to this novel class of drugs, Stewart Tepper, MD, a headache specialist and clinical researcher at Dartmouth College, was quoted by *The New York Times* saying, "So far they look fantastic. They shake the ground under our feet. They will change the way we treat migraine."[7]

The FDA approval of erenumab also represents a major milestone in headache research because it is the first mechanism-specific preventive treatment explicitly designed for migraine rather than serendipitously stumbled upon.[8] Among thousands of patients tested across multiple clinical trials, the safety and tolerability of the monoclonal antibodies to CGRP and CRP receptors are unparalleled among migraine preventive therapies to date. This is critically important, because it is estimated that >70% of oral preventive medicines for migraine are discontinued within 6 months of initiation, primarily because of side effects. Safe, convenient, and well-tolerated preventive treatments are likely to improve medication adherence.

The Future

Looking ahead, CGRP-blocking agents may treat other headache types and not just migraine. For example, the CGRP ligand monoclonal antibody galcanezumab (Lilly, Indianapolis, IN) has been shown to be safe and effective for the prevention of episodic cluster headache in adults,[9] and several companies are studying CGRP-related monoclonal antibodies in chronic posttraumatic headache. By the end of the year, more CGRP-related monoclonal antibodies will follow erenumab, and after that, the small-molecule CGRP antagonists will be upon us, along with 5-HT_{1F} agonists. Soon there will be a panoply of new and exotic vocabulary in our lexicon: ubrogepant, rimegepant, atogepant, galcanezumab, eptinezumab, fremenezumab, PACAP, and lasmitidan.

You'd be hard-pressed to find any more exciting subspecialty in neurology lately than headache medicine.

We Are All Headache Specialists

More than 2% of people globally have a form of primary headache. Migraine is by far the most common disorder neurologists treat and the second most disabling after stroke. Many people with migraine will agree, at least with tongue planted firmly in cheek, that the fact that migraine doesn't kill you is a mixed blessing. Although this is true, migraine has a profound impact on daily living. A person with 8 migraine days a month has to live with nearly 100 days per year of moderate-to-severe pain, nausea, cognitive changes, and major disruption of all that is important, necessary, and fun in life. We neurologists can change this, but to do so, we must want to collectively.

There are not, and never will be, enough board-certified headache specialists to care for all patients with headache. This is not cause for fear! You don't need UCNS board certification to be a terrific headache doctor; it simply takes enthusiasm, a sufficient knowledge base, and the desire to take the discipline and those who suffer from disabling head pain seriously. With new, targeted treatment options and increased understanding of pathophysiology, we need head-

ache practitioners now more than ever. We need stroke neurologists, neuro-oncologists, movement disorder specialists, epileptologists, and neurocritical care specialists, and they can and should also be well-versed in treating headache. Our colleagues in emergency medicine and primary care also need to understand headache basics, for they are the first lines of defense.

The good news is it's a tremendously exciting time to brush up on the burgeoning world of headache medicine and learn a few new things too. This field is evolving, transforming, and growing like never before. The goal for this column is to document and comment on this rapid progress and change, doing our small part to educate neurologists and others on this important group of pain disorders and generate excitement about headache medicine.

Future columns will take deeper dives into diverse and timely topics, including pharmacological treatment, stigma, neurostimulation, complementary and alternative modalities, controversies, comorbidities, and divergent opinions. For good measure, we'll throw in sex (coital headaches), drugs (medical marijuana, anyone?), and rock and roll (loud music linked to increased headaches in teens[10]) whenever possible.

In such a pivotal paradigm-shifting epoch, it seems reasonable and proper to paraphrase the French newspaper *Le Monde* in the immediate aftermath of the September 11th attacks: *Aujourd'hui, nous sommes tous specialists des maux de tête!* Today, we are all headache specialists!

Welcome to this inaugural edition! ■

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