Spinal Cerebrospinal Fluid Leak — An Under-recognized Cause of Headache
More common than expected, why is this type of headache so often misdiagnosed or the diagnosis is delayed?

Challenging the “One Size Fits All” Approach in Modern Medicine
As research becomes more patient-centric, it is time to recognize individual variations in response to treatment and determine why these differences occur.

Newly Approved CGRP Blocker, Aimovig™, the First Ever Migraine-Specific Preventive Medicine
The approval of erenumab and eventually, other drugs in this class heralds a new dawn for migraine therapy. But will it be accessible for patients who could respond to it?

Remembering Donald J. Dalessio, MD

The Headache Clinic
Featuring the Baylor Scott & White Headache Clinic in Temple, Texas.

An Excerpt from the New Book –
Headache Solutions at the Diamond Headache Clinic
Written by Doctor Diamond in collaboration with Brad Torphy, MD.
If you think a headache is just a headache, think again. Millions of Americans suffer from migraines, cluster headaches, and other serious headache disorders. Chances are, headache disorders affect you or someone you love.

Join the cause by donating to the National Headache Foundation, the world’s largest voluntary organization for the support of people with migraine and headache disorders. For 48 years, the NHF has assisted millions of individuals and inspired hope through awareness, advocacy, education, and research.

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FROM THE EXECUTIVE CHAIRMAN:

The National Headache Foundation was founded in 1970, and we have observed many changes in headache therapy over the years. As was in the beginning, we are committed to those experiencing headache. Our Mission is “To Cure Headache and End Its Pain and Suffering,” and our Vision is “A World Without Headache.” Recent events have brought our goals closer to fruition.

For the last few years, the CGRP (calcitonin gene-related peptide) pathway in migraine has been explored. This research has been targeted in efforts to identify new treatments for migraine disease. Recently, a monoclonal antibody therapy, based on the CGRPs, has been approved by the Food and Drug Administration. The National Headache Foundation applauds Amgen and Novartis, the manufacturers of Aimovig™ (erenumab), for their achievement in being the first anti-CGRP agent to reach patients.

Several pharmaceutical companies are currently in development of anti-CGRPs, including Eli Lilly (galcanezumab), Teva (fremanezumab), and Alder (eptinezumab). Erenumab, galcanezumab, and fremanezumab will be administered by subcutaneous injection. Eptinezumab is being developed for intravenous administration. Ubrogepant (Allergan) and rimegopant (Biohaven) are being studied as oral preparations of anti-CGRPs. Our hopes are that these new agents will revolutionize headache therapy.

In this issue, Timothy Smith, MD, R.Ph., the first Vice President of the NHF, has contributed an article which reviews these therapies and their potential benefits for those experiencing migraine. At the NHF, we are significantly encouraged that the anti-CGRPs will help a great number of the 40 million Americans with migraine disease.

Seymour Diamond, M.D.
Chicago, Illinois
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Spinal Cerebrospinal Fluid Leak – An Under-recognized Cause of Headache
Misdagnosis and delayed diagnosis of spontaneous intracranial hypotension, or low cerebrospinal fluid (CSF) pressure inside the head, is common. It is an under-recognized cause of headache that is treatable and in many cases, curable. Raising awareness of this condition can improve the situation for these patients.

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Challenging the “One Size Fits All” Approach in Modern Medicine
The variation between individuals in their migraine risk factor profiles demonstrates that everybody is different on a risk susceptibility level. But will we ever be able to understand the mechanisms driving these differences and relate them to individual therapeutic response?

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Newly Approved CGRP Blocker, Aimovig™, the First Ever Migraine-Specific Preventive Medication
In May, 2018, erenumab (Aimovig™) was approved by the Food and Drug Administration for use in migraine preventive therapy. This drug and other agents in this category hold promise for many patients who are most impacted by disabling headaches.

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Obituary and Remembrance – Donald J. Dalessio, MD
On February 25, 2017, former National Headache Foundation Board President and member, Donald J. Dalessio, MD, passed away at his home in La Jolla, California. Our Executive Chairman, Seymour Diamond, MD, recalls his long friendship and collaboration with this early leader in headache medicine.

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Book Excerpt – The Ex-infantryman
We present an excerpt from the new book, Headache Solutions at the Diamond Headache Clinic, by Seymour Diamond, MD with Brad Torphy, MD.
Former National Headache Foundation Board member, Donald J. Dalessio, MD, passed away on February 25, 2017 at his home in La Jolla, California. Doctor Dalessio was a member of the Board from May, 1971 through June, 1980, and again from February, 1998, through February, 1999. He served as President of the NHF from October, 1977 through March, 1980.

A native of New Jersey, Dr. Dalessio attended Wesleyan University, Middletown, CT, and was a 1956 graduate of Yale Medical College, New Haven, CT. Following his graduation from Yale, Dr. Dalessio completed an internship at New York City (Cornell) Medical Center, where he trained in neurology and medicine, and worked with Dr. Harold G. Wolff, the noted headache researcher. He then became the Resident in Medicine at the Yale Medical Center. For several years, Dr. Dalessio served as a Captain in the United States Army.

For many years, he served as Chairman of the Medicine Group and Senior Consultant in Neurology at Scripps Clinic and Research Foundation in La Jolla. Upon his retirement from active practice, his colleagues at Scripps Medical Center renamed the headache clinic – The Donald J. Dalessio Headache Center at Scripps Clinic.

Dr. Dalessio wrote and/or edited multiple editions of Wolff’s Headache, a standard text used by health care practitioners in the U.S. and internationally. He had served as editor of Headache, the journal of the American Association for the Study of Headache (now the American Headache Society) and the Scripps Clinic Personal Health Newsletter. He served on the Editorial Board of JAMA (Journal of the American Medical Association), and was also a Medical Columnist for the San Diego Tribune.
Donald J. Dalessio, MD

The first time that I met Donald Dalessio was at the American Association for the Study of Headache (now the American Headache Society) meeting in 1964. The following year, Don became editor of the journal, Headache. Up to that time, the journal had been a failing publication. Don served as Editor for over 20 years, upgrading the publication to its status as a recognized, peer-reviewed journal. He took a hiatus from editorial responsibilities, from 1974 to 1976, when he served as President of the AASH.

At that meeting in 1964, Don and I began a friendship that persevered for many years. In 1970, he helped me establish the National Migraine Foundation (now the National Headache Foundation). With his wife, Jane, he helped start the Foundation’s monthly newsletter that survives to this day.

In 1973, we served as co-editors of the textbook, The Practicing Physician’s Approach to Headache. This collaboration continued through five editions, and in 1998, the sixth edition was renamed, Diamond and Dalessio’s The Practicing Physician’s Approach to Headache, which was edited by Merle Diamond and Glen Solomon. These editions became standard texts for those health care practitioners managing headache patients.

Starting in 1987, Don served as my Co-Director for the continuing medical education courses of the Diamond Headache Clinic Research & Educational Foundation in Palm Springs. In 1993, we added a summer course at DisneyWorld in Florida. These courses became one of the most successful programs in headache medicine.

The courses provided opportunities for both of our families, including grandchildren, to interact – no matter where the course was being held. Elaine and I always looked forward to socializing with the Dalessio clan.

We consider it our good fortune to have known Don Dalessio and to call him our friend and colleague. He will be truly missed.

Seymour Diamond, MD
It is a myth. It is not true that headache victims are somehow, in ways subtle or obvious, weaker than the rest of us. It is not true that they collapse under stress. It is simply that they are attacked by a particular kind of pain for reasons which they themselves cannot altogether recognize.

About 20 years ago, Gregory Wilson was a squarely built, chesty man of fifty who wore his authority with easy assurance. His black bushy hair was edged with gray. He talked in short staccato phrases. His father was one of the most famous men in journalism and he himself had built a formidable career in business: he was one of the top public relations men in one of the largest corporations in the United States. He was a hard-driving man who liked to busy himself outside of his job with other writing projects. He was as successful in them as he was in the rest of his career.

Some 16 years ago, he had been attacked by severe and recurring headaches. There is every indication that he had a migraine personality and he, for one, was convinced that they were migraine. He remained convinced of that, although I disagreed with him.

Although he was in a stress-filled job, he was not easy prey to stress of an exceptional kind. He had been a combat infantryman during two tours in Vietnam, and he suffered no particular stress under the most violent conditions. He did not even suffer from lack of sleep.

Early in the 1990s, he took a year’s leave of absence from work to run for Congress. It did nothing but make him feel better. “Despite a grueling 16-hour day, 7-days-a-week schedule of campaigning which taxed mind and body, I never had a single headache, upset stomach, or sleepless night,” he said. “The increased work load and responsibility made me peppier than ever before in my life.”

He was in his early thirties when the headaches first became burdensome. He checked with his company physician, underwent a detailed checkup, and found that he was a diabetic. That was a strange in terms of migraine action. Diabetics are likely to find that their migraine is reduced, not increased, with the onset of the disease. “I believe your headaches are due to tension,” the doctor reported to him. But once the belief was stated, the relief did not follow.

Over the years, he consulted a good many distinguished physicians in New York, Chicago, and elsewhere to seek help for his headaches, but none was forthcoming. One winter he was vacationing in Tucson, Arizona, where he went to an excellent physician for both headaches and diabetes. The doctor gave him a long technical article on headaches to read and he found my name mentioned. He found it again when he returned home and read a story on headaches by a science writer. He knew the writer involved, so he checked me out, and then arranged for an appointment.

We gave him the in-office physical. He’d just had a very extensive battery of hospital tests. Fearful of a brain tumor, he’d checked into one the finest hospitals in Chicago and come out with a report that he was free of tumor or other abnormalities in the brain and skull. But he still had his headaches.

Between the hospital reports and my in-office procedures, we were able to eliminate organic problems as a cause of his headaches. As for his diabetes, he was taking a bedtime dose of long-acting insulin glargine (Lantus). He reported that his blood glucose was under control.

We are including an excerpt from the book, Headache Solutions at the Diamond Headache Clinic. The book was written by Doctor Diamond in collaboration with Brad Torphy, MD. The book is available for purchase at Amazon.
He was convinced that he had migraine. That was understandable, but I began to look elsewhere, for his headaches were not focused on one side or the other. They came daily, not occasionally. He was troubled by sleep disturbances – he customarily awakened early in the morning. All these were signs of a deep depression that was exhibiting itself in a persistent and intense headache. Actually, I felt he was getting chronic daily headaches. For though the depression was prominent, some of the headaches he suffered, on occasion, to me sounded very much as if they were migraine. So I chose the monoamine oxidase inhibitor (MAOI) – phenelzine (Nardil). I had two reasons for choosing phenelzine: It is one of those rare medications which seem to work against depression as well as against migraine; and I did not want to use the common antidepressants, amitriptyline (Elavil), for example, because I felt it might cause complications with his diabetes. It turned out that the choice was a good one. His headaches were greatly reduced right from the start. As time went by, he seemed to overcome them altogether. He saw other benefits from the medication. “I no longer lose my temper over sloppy work and my patience quota has risen sharply,” he said.

But the second phase of treatment failed somewhat. I was, of course, curious professionally and personally at what might be causing the depression. For here was a man who had endured combat and politics without any headache problems or sleep disturbance. And suddenly in his thirties and forties he fell prey to both. I thought it might have to do with his married life. There were indications that he was not getting on well with his wife and some of the headache patterns – their increase during vacations and weekends – suggested an effort to maintain calm in a situation which he found difficult. But when I asked him about it, he was quite blunt. He didn’t want to talk about it. He told me he didn’t consult me as a psychiatrist. Thus, the barriers were high and formidable. When somebody tells me that, I leave him alone.

We’d conquered the pain, and that was his top concern. He was aware, I’m sure, of the conflict that brought about depression. And he was learning to live with it or to live apart from it: he separated from his wife. He was not a weak man; his whole life showed that, and once he was freed from pain, he was also free to tackle, by himself, the problem behind it.

In subsequent years, whenever my name appeared in relation to headache he would send me a note and a copy of the article and tell me in his note how well he was doing. He died recently of other causes than his headache but donated a very substantial amount of his fortune to the National Headache Foundation. HW
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BOTOX® prevents on average 8 to 9 headache days and migraine/probable migraine days a month (versus 6 to 7 for placebo).

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Indication
BOTOX® is a prescription medicine that is injected to prevent headaches in adults with chronic migraine who have 15 or more days each month with headache lasting 4 or more hours each day in people 18 years or older. It is not known whether BOTOX® is safe or effective to prevent headaches in patients with migraine who have 14 or fewer headache days each month (episodic migraine).

IMPORTANT SAFETY INFORMATION
BOTOX® may cause serious side effects that can be life threatening. Get medical help right away if you have any of these problems any time (hours to weeks) after injection of BOTOX®:

● Spread of toxin effects. The effect of botulinum toxin may affect areas away from the injection site and cause serious symptoms including: loss of strength and all-over muscle weakness, double vision, blurred vision and drooping eyelids, hoarseness or change or loss of voice, trouble saying words clearly, loss of bladder control, trouble breathing, trouble swallowing.

Please see additional Important Safety Information on adjacent page.

¹Truven Health MarketScan Data, November 2010–April 2017.
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IMPORTANT SAFETY INFORMATION (Continued)

There has not been a confirmed serious case of spread of toxin effect away from the injection site when BOTOX® has been used at the recommended dose to treat chronic migraine.

BOTOX® may cause loss of strength or general muscle weakness, vision problems, or dizziness within hours to weeks of taking BOTOX®. If this happens, do not drive a car, operate machinery, or do other dangerous activities.

Do not receive BOTOX® if you: are allergic to any of its ingredients (see Medication Guide for ingredients); had an allergic reaction to any other botulinum toxin product such as Myobloc® (ribobotulinumtoxinB), Dysport® (abobotulinumtoxinA), or Xeomin® (incobotulinumtoxinA); have a skin infection at the planned injection site.

The dose of BOTOX® is not the same as, or comparable to, another botulinum toxin product.

Serious and/or immediate allergic reactions have been reported, including itching, rash, red itchy welts, wheezing, asthma symptoms, or dizziness or feeling faint. Get medical help right away if you experience symptoms; further injection of BOTOX® should be discontinued.

Tell your doctor about all your muscle or nerve conditions such as ALS or Lou Gehrig’s disease, myasthenia gravis, or Lambert-Eaton syndrome, as you may be at increased risk of serious side effects including difficulty swallowing and difficulty breathing from typical doses of BOTOX®.

Tell your doctor about all your medical conditions, including if you: have or have had bleeding problems; have plans to have surgery; had surgery on your face; weakness of forehead muscles; trouble raising your eyebrows; drooping eyelids; any other abnormal facial change; are pregnant or plan to become pregnant (it is not known if BOTOX® can harm your unborn baby); are breastfeeding or plan to (it is not known if BOTOX® passes into breast milk).

Tell your doctor about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. Using BOTOX® with certain medicines may cause serious side effects. Do not start any new medicines until you have told your doctor that you received BOTOX® in the past.

Tell your doctor if you received any other botulinum toxin product in the last 4 months; have received injections of botulinum toxin such as Myobloc®, Dysport®, or Xeomin® in the past (tell your doctor exactly which product you received); have recently received an antibiotic injection; take muscle relaxants; take allergy or cold medicines; take sleep medicine; take aspirin-like products or blood thinners.

Other side effects of BOTOX® include: dry mouth, discomfort or pain at injection site, tiredness, headache, neck pain, eye problems: double vision, blurred vision, decreased eyesight, drooping eyelids, swelling of eyelids, dry eyes; and drooping eyebrows.

For more information refer to the Medication Guide or talk with your doctor.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch or call 1-800-FDA-1088.

Please refer to the Summary of Information about BOTOX® on the following page.
Summary of Information about BOTOX®
(onabotulinumtoxinA)

What is the most important information I should know about BOTOX®?

BOTOX® may cause serious side effects that can be life threatening. Call your doctor or get medical help right away if you have any of these problems any time (hours to weeks) after injection of BOTOX®:

- Problems swallowing, speaking, or breathing, due to weakening of associated muscles, can be severe and result in loss of life. You are at the highest risk if these problems are pre-existing before injection. Swallowing problems may last for several months.
- Spread of toxin effects. The effect of botulinum toxin may affect areas away from the injection site and cause serious symptoms including: loss of strength and all-over muscle weakness, double vision, blurred vision and drooping eyelids, hoarseness or change or loss of voice, trouble saying words clearly, loss of bladder control, trouble breathing, trouble swallowing.

There has not been a confirmed serious case of spread of toxin effect away from the injection site when BOTOX® has been used at the recommended dose to treat Chronic Migraine.

BOTOX® may cause loss of strength or general muscle weakness, vision problems, or dizziness within hours to weeks of taking BOTOX®. If this happens, do not drive a car, operate machinery, or do other dangerous activities.

BOTOX® dosing units are not the same as, or comparable to, any other botulinum toxin product.

What is BOTOX®?

BOTOX® is prescription medicine a medical professional injects into muscles to prevent headaches in adults with Chronic Migraine who have 15 or more days each month with headache lasting 4 or more hours each day in people 18 years and older.

It is not known whether BOTOX® is safe or effective to prevent headaches in people with migraine who have 14 or fewer headache days each month (episodic migraine).

Who should not take BOTOX®?

Do not use BOTOX® if you are: allergic to any of the ingredients in BOTOX® such as botulinum toxin type A and human serum albumin; had an allergic reaction to another botulinum toxin product such as Myobloc® (rimabotulinumtoxinB), Dysport® (abobotulinumtoxinA), or Xeomin® (incobotulinumtoxinA); or have a skin infection at the planned injection site.

What should I tell my doctor before treatment?

Tell your doctor about all your muscle or nerve conditions, such as amyotrophic lateral sclerosis (Lou Gehrig's disease), myasthenia gravis, or Lambert-Eaton syndrome, as you may be at increased risk of serious side effects.

Tell your doctor if you have or have had breathing problems such as asthma or emphysema; swallowing problems; bleeding issues; plan to or have had surgery; have forehead muscle weakness such as trouble raising your eyebrows; drooping eyelids; or any changes to your face.

Tell your doctor if you are pregnant, plan to become pregnant, are breastfeeding or plan to breast feed. It is not known if BOTOX® (onabotulinumtoxinA) can harm your unborn baby or if BOTOX® passes into breast milk.

What Are Common Side Effects?

The most common side effects include neck pain; headache; migraine; slight or partial facial paralysis; eyelid drooping; bronchitis; musculoskeletal stiffness; muscular weakness; pain in 1 or more muscles, ligaments, tendons, or bones; muscle spasms; injection site pain; and high blood pressure. Other side effects have been reported including allergic reactions e.g. itching, rash, red itchy welts, wheezing, asthma symptoms, or dizziness or feeling faint.

These are not all of the possible side effects. Call your doctor for medical advice if you experience any side effects after treatment with BOTOX®.

What Should I Tell My Doctor About Medicines and Vitamins I Take?

Using BOTOX® with certain medicines may cause serious side effects. Do not start any new medicines until you have told your doctor that you have received BOTOX® in the past. Tell your doctor if you have received an injection with another botulinum toxin product in the last 4 months, such as Myobloc®, Dysport®, or Xeomin®. Be sure your doctor knows which product you received.

Tell your doctor about all prescription and over-the-counter medicines and supplements you take including: vitamins and herbal products; recent antibiotic injections; anticholinergics; muscle relaxants; allergy or cold medicine; sleep medicine; aspirin-like products; and blood thinners. Ask your doctor if you are not sure whether your medicine is listed above.

To Learn More

If you would like more information, talk to your doctor and/or go to BotoxChronicMigraine.com for full Product Information.

You may report side effects to the FDA at www.fda.gov/medwatch or call 1-800-FDA-1088.

Based on 72511US15 Rev. 01/2016

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Allergan
HEMIFACIAL SPASMS

I have developed severe hemifacial spasms. They create a constant headache and seem to be sparking migraines as well. What is the connection? I have tried gabapentin, Botox injections, massage and acupuncture with no positive results. What other possible treatments could possibly work? – Dorene

I have to assume that this is the correct diagnosis, but hemifacial spasm is by itself painless. It is usually treated with Botox, but that needs to be administered by someone with great expertise in treating that condition. Carbamazepine and baclofen are medications that sometimes help. We always order a MRI scan in this condition to make sure that there isn’t something, like a blood vessel loop, compressing the facial nerve in the brain (pons).

Mark W. Green, MD
Mount Sinai Hospital
New York, NY

FERMENTED FOODS AND HEADACHE

I was wondering if raw organic (unfiltered) apple cider vinegar would be ok for a migraineur like me? I was told apple cider vinegar is generally made from crushed apples, but bacteria and yeast are added to ferment the liquid. I know to avoid fermented food and drinks, so I would like to make sure if it’s ok. – Janet H.

Fermented foods that contain tyramine (caused by the breakdown of the amino acid tyrosine) are usually problematic in migraine patients that are on specific medications that interact with tyramine, particularly MAOI inhibitors. Apple cider vinegar has been mentioned as a possible home-based therapy for migraine, although there is no clear scientific evidence that it helps. It is unlikely that the unfiltered apple cider vinegar will trigger a migraine and is o.k. to try in a migraineur.

George R. Nissan, D.O.
Plano, TX

HEADACHE AND SCHOOL

Why do I always get headaches as soon as I go to school? I’m a 17-year-old high school student and most days I get some sort of headache. – Dylan H.

Headaches are a threshold phenomenon, meaning that anybody can get a headache in the setting of enough triggers. There are many reasons why the school day can be the thing that pushes people over the edge in terms of getting a headache, but it usually isn’t the only trigger at play. For example, factors like quality of sleep the night before, quantity and frequency of caffeine use, hydration status, pattern of not eating breakfast or skipping meals, hormonal fluctuations during your menstrual cycle, regularity of exercise, overuse of pain medication and stress of school are all examples of triggers that may factor in to whether or not you get a headache. That being said, anyone who is getting headaches on a frequent basis should see her doctor for a thorough evaluation to make sure there aren’t other underlying medical reasons for headaches. The most important thing to do is to begin keeping a diary of your headaches so that you can track when they happen.
and begin noticing what your personal headache triggers are. Once you have that information you can begin controlling those triggers you do have control over (e.g. like staying well-hydrated with at least 1.5-2 Liters of non-caffeinated fluid daily, and not going long periods without eating).

Sarah Rahal, MD
New York, NY

MAGNESIUM AND HEADACHES

I’m 71 years old and I’ve had migraine with aura for years. Recently, I was told that my migraines may be related to a lack of magnesium. Could using magnesium help? – Ruby

Magnesium deficiency is very common in patients with migraines. Additional symptoms of magnesium deficiency include feeling cold or having cold hands and feet, leg muscle cramps, palpitations, and other. Ideally, have your doctor check your red blood cell (RBC) magnesium level and if it is low or at the low end of normal, you could greatly benefit from taking a supplement. RBC magnesium test is available at all laboratories and is much more accurate than the more popular serum magnesium test. If you do not want to have a blood test or your doctor does not want to order RBC magnesium level, you could just try taking 400 mg of magnesium daily. There are different types of magnesium and one of the better absorbed ones is magnesium glycinate. Some people don’t absorb magnesium well and need more than 400 mg a day or even require monthly infusions. The only side effect that sometimes occurs with oral magnesium is stomach upset or diarrhea and that is why it should be taken with food. The only patients who are at risk of getting too much magnesium, which can be dangerous, are those with serious kidney problems. It is best to check with your doctor before you start taking any supplements.

Alexander Mauskop, MD
New York, NY

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Spontaneous intracranial hypotension, or low cerebrospinal fluid (CSF) pressure inside the head, is an under-recognized cause of headache that is treatable and in many cases, curable. Although misdiagnosis and delayed diagnosis remain common, increasing awareness of this condition is improving the situation for those afflicted.

Frequently, patients with a confirmed diagnosis of intracranial hypotension will report that they have been treated for chronic migraine or another headache disorder for months or years. This type of headache rarely responds to medications; however, when treatment is directed at the appropriate underlying cause, most patients respond well.

**Anatomy of Intracranial Hypotension**

In almost all cases, intracranial hypotension results from a leak of cerebrospinal fluid at the level of the spine. Spontaneous CSF leaks located at the level of the skull base that leak from nose or ear are not causally associated with intracranial hypotension.

Low pressure headache is a term commonly used for the headache resulting from intracranial hypotension. It is important to note that a significant percentage of patients have normal cerebrospinal fluid pressure measurements. Our understanding has evolved to recognize that a low volume of the cerebrospinal fluid is the core problem although pressure is related to volume.

The cerebrospinal fluid surrounds the brain and spinal cord in one continuous compartment. One of its many functions is to cushion the fatty brain which floats in this watery fluid. The fluid is held in place by a tough connective tissue layer called the dura mater, or simply the dura. A hole or tear of the spinal dura results in the loss of cerebrospinal fluid volume around the brain and spinal cord, and sinking of the brain inside the head. When the patient is lying flat, the cerebrospinal fluid pressure in the head and the spine are equal. However when the individual is upright, the cerebrospinal fluid pressure in the head is much lower than the pressure in the lower spine, as with any column of fluid. When a loss of cerebrospinal fluid volume occurs, this results in a larger than normal drop in pressure in the head when the patient goes from lying flat to being upright. This pressure change during positioning explains why symptoms are usually worse when the patient is upright.
The Headache

The most common symptom associated with intracranial hypotension is an “orthostatic” or positional headache. When the patient rises from lying flat, the pain often worsens within seconds to hours and improves with lying flat again. When severe, the patient may be unable to raise their head even one inch off the bed or may need to position their head lower than their spine for relief. This positional aspect tends to be more abrupt soon after the onset of the leak, and may become less evident over time. The headache may evolve into a “second-half-of-the-day headache” or a chronic daily headache without an obvious postural component. It is very common for patients with intracranial hypotension due to a spinal CSF leak to be misdiagnosed with migraine headache, cervicogenic headache, occipital neuralgia, or another headache disorder.

Usually, the headache is daily but in some cases, may be intermittent. The pain is located most often at the back of the head, but may be at both temples, across the front of the head, or all over the head. Severity can range from mild to excruciating. The headache quality may be variably described as pulling, pressure, or throbbing.

Some patients remain quite functional despite their symptoms while others have very limited ability to be functional when sitting or standing upright. Patients may be largely bedridden. The degree of disability is often under-appreciated.

Headache is not universally prominent or even present. A range of other symptoms may be more troublesome than head pain for a subset of patients.

Other Symptoms

Patients with intracranial hypotension often report neck pain or stiffness, nausea with or without vomiting, pain or tightness between the shoulder blades, sense of being off balance, changes in hearing, dizziness or vertigo, sensitivity to light or sounds, cognitive difficulties, as well as arm pain or numbness. Less commonly reported symptoms include visual changes, facial pain or numbness, fatigue, changes in taste, pain at nerve root levels below the shoulders, or fluid discharge from the nipples. More rare presentations or complications include unsteady gait, tremor, dementia, quadriplegia, stroke, stupor/coma, and very rarely, death.
Spinal Cerebrospinal Fluid Leak
– An Under-recognized Cause of Headache

Underlying Causes

**Spontaneous**

The cases that occur with no apparent precipitating event or a relatively minor physical factor, such as lifting or bending, are the type that most often remain unrecognized for months or years. There are two known associations with spontaneous spinal CSF leaks. Patients may have an underlying weakness of the spinal dura from an inherited disorder of connective tissue, including but not limited to Ehlers-Danlos syndromes and Marfan syndrome. The second known association is underlying bone spurs arising from calcified intervertebral (between the vertebrae) discs. These bone spurs can puncture the spinal dura.

Spontaneous leaks may occur at any age and in both genders but are diagnosed more often in women around age 40. An estimated incidence of 5 in 100,000 per year is based on a single study of patients presenting to an emergency department and is probably an underestimate since most patients are now diagnosed on an outpatient basis.

**Medical Procedures**

The most common cause of a spinal CSF leak is a lumbar puncture (spinal tap), in which the spinal dura is intentionally punctured for diagnostic or therapeutic reasons. A positional headache that develops after the procedure is usually recognized and treated promptly.

Another well-known cause of a spinal CSF leak is an inadvertent puncture of the spinal dura during an epidural anesthesia or an epidural steroid injection. These injections normally go into the space inside the spinal canal but outside the dura.

Spinal surgery can be complicated by nicks or tears of the spinal dura. These leaks may or may not be recognized promptly.

Over-draining CSF shunts are also known to cause intracranial hypotension.

**Trauma**

Cerebrospinal fluid leaks have been reported in association with injuries sustained in falls, motor vehicle accidents, or sports injuries.

Spontaneous intracranial hypotension, or low cerebrospinal fluid (CSF) pressure inside the head, is an under-recognized cause of headache that is both treatable and in many cases, curable.
Diagnosis

The diagnosis of intracranial hypotension relies primarily on the symptoms and history of the patient. The positional aspect of the headache is a key feature in most, but not all, cases. A patient may report a recent history of a lumbar puncture, epidural anesthesia or injection(s), surgery, or trauma. A previous diagnosis of postural orthostatic tachycardia syndrome (POTS) is not uncommon. POTS refers to a condition in which moving from a lying to standing position causes an abnormal increase in heart rate and a range of other signs and symptoms. A patient’s positional symptoms may be due to POTS or due to a spinal CSF leak or both. Underlying inherited disorders of connective tissue (Marfan syndrome, Ehlers-Danlos syndromes, others) may or may not be recognized prior to the onset of symptoms related to a spinal CSF leak. A few patients may have received a diagnosis of Chiari I due to the brain imaging finding of low-lying cerebellar tonsils (part of brain at back of head). Chiari I is a congenital condition in which the back part of the skull is abnormally small or misshapen, and part of the brain, the lower part of the cerebellum, extends into the spinal canal. In intracranial hypotension, the finding of low lying cerebellar tonsils and brain sag is due to the loss of CSF volume and is reversible with treatment of the leak, so it is often called pseudo-Chiari. It can be challenging for clinicians to sort out if this finding on brain imaging is from congenital Chiari or from low CSF volume of intracranial hypotension or from a combination of both. Minimal response to medications used for migraines can be an additional clue to the diagnosis.

A diagnostic lumbar puncture to determine pressure measurement or CSF analysis is not usually performed unless another disorder such as meningitis is being ruled out. Minor CSF abnormalities may be noted and cerebrospinal fluid pressure may be low, normal, or even high.

An MRI of the brain with contrast should be done in all suspected cases to determine several classic findings although imaging findings are absent in about 20% of patients. Spinal imaging is used to locate leaks or other abnormalities for targeted treatment – but may be negative in up to one-half of suspected cases due to the limits of sensitivity. A full spine MRI without contrast is often the initial choice because the testing is non-invasive. Myelography, which involves lumbar puncture for the injection of contrast, uses CT, MR, or digital subtraction techniques. More than one type of spinal imaging is often needed.

**DIAGNOSTIC CHALLENGES**

- low awareness contributes to delayed diagnosis and misdiagnosis
- not every headache due to intracranial hypotension is positional
- not every positional headache is due to intracranial hypotension
- not every patient with intracranial hypotension has a headache
- common and uncommon presentations and findings may not be recognized as secondary to intracranial hypotension (subdural hematomas, tremor, unsteady gait, dementia, low lying cerebellar tonsils, coma, stroke, spinal cord manifestations)
- normal CSF pressures are not uncommon
- imaging interpretation requires experience and training
- brain MRI is normal in ~ 20%
- spinal imaging is negative in ~ 50%
- more than one type of spinal imaging is often needed

Most patients who receive treatment for intracranial hypotension do well, with improved quality of life or complete cure.
Treatments

Spinal CSF leaks associated with medical procedures are amenable to targeted treatment approaches.

It is suspected that a substantial percentage of spontaneous cases resolve within days to weeks of onset without any intervention. A brief course of a conservative approach is often recommended if symptom severity and complications do not preclude it. Consuming extra fluids and generous amounts of caffeine, as well as bedrest may reduce symptom severity. Medications often used for migraine headaches are largely ineffective for the head pain. Treatment directed to the underlying cause of spinal CSF leak is needed when conservative measures fail.

Urgent treatment will be needed in cases with serious complications, such as coma or a large subdural hematoma (blood clot pressing on brain inside the skull).

Epidural blood patch (EBP) is a procedure used routinely for post-dural puncture headache and is also the mainstay of treatment for spontaneous spinal fluid leaks. This may be performed after brain MRI with contrast but with or without imaging of the spine. This imaging-guided procedure involves the injection of the patient’s blood into the epidural space (space just outside the dura) in the lumbar and/or thoracolumbar region of the spine. It may be repeated several times.

If the response to one or more epidural blood patches is partial or if the symptoms relapse, spinal imaging is performed to try to locate the leak for targeted treatment. If evident on imaging, the leak location and characteristics will dictate the best approach, whether that be epidural patching targeted to the level of the leak or open surgical repair. Targeted epidural patching is done with blood, fibrin sealant (type of glue made from blood products), or both. When spinal imaging is negative, non-targeted epidural blood patches may be repeated or epidural patching may be targeted at suspected leak locations.

Surgical repairs are necessary for some patients depending on factors such as the leak type, leak location, or for patients in whom other measures have failed.

Prognosis

Following successful treatment, some patients develop rebound intracranial hypertension or elevated intracranial pressure. This scenario is usually self-limited but may last for weeks or months, rarely for years. Treatment with medications to lower intracranial pressure is occasionally necessary.

While study of long-term outcomes remains limited, most patients who receive treatment for intracranial hypotension do well, with improved quality of life or a complete cure. Negative spinal imaging, however, limits treatment options for those with partial or temporary response to epidural patching procedures. There are patients, however, that endure persistent symptoms despite multiple procedures.

Summary

A significant percentage of individuals with chronic daily headache may actually be suffering from intracranial hypotension secondary to a spinal CSF leak. These individuals tend to have minimal response to treatments normally used for primary headache disorders. Treatment directed at the underlying cause can lead to improved quality of life or a complete cure. As awareness of this disorder rises, diagnostic delays are becoming shorter. Earlier diagnosis and treatment are critical to reducing the burden of suffering.

Recommended Reading


Spinal CSF Leak Foundation Resources. http://spinalcsfleak.org/resources

We can easily recognize the face of someone we know from thousands, if not millions, of other humans. However, it turns out that individual differences in physical appearance are dwarfed by the biochemical differences within us. In the middle of the last century, Roger J. Williams, PhD, a distinguished American scientist specializing in nutrition at University of Texas, argued eloquently that clinically speaking, the “average man” simply does not exist. Indeed, he said the very hallmark of being human is the high degree of individual variation our species exhibits.

The variability that Dr. Williams referred to went beyond the obvious differences or even the presence or absence of a single genetic change that can alter drug response. Dr. Williams wrote: “If normal facial features varied as much as gastric juices do, some of our noses would be about the size of navy beans while others would be the size of twenty-pound watermelons.”

Beneath this witty statement lies something less obvious and very intriguing. What Dr. Williams may be alluding to is the fact that in human evolution, millions of years of sexual selection and the desire to have mates that don’t look odd, may have acted to greatly normalize our physical appearance. Beneath our physical appearance however, our internal anatomy and biochemical machinery were never subject to such a normalizing selection pressure. Therefore, we may be greatly underestimating the anatomical and biochemical diversity that lies beneath our skin.

Today only one of his books remains in print, but at the time Dr. Williams’ studies were widely published and the importance of his work was embraced by some of...
the world’s greatest thinkers including the writer Aldous Huxley and the biochemist Linus Pauling, PhD (the only person to win two unshared Nobel prizes).1

And today, more than 50 years later, the medical community lacks the tools to embrace the “everybody is unique” paradigm. The current state of the industry prompts three questions. Where did our current medical “one size fits all” approach come from? How effective is it if we develop medicines for Mr. or Ms. Average? And if it is not, how could we move on to a more effective approach?

The answer to the first question revolves around the tendency to aggregate populations of people and average things into a single number (or set of numbers) that may not be representative of any individual. If other industries used this approach they would go out of business fairly rapidly. Imagine if the clothing industry only offered one size fits all.

The time in Western history when we became interested in dealing with populations of people and stamping out something that could be sold to entire populations was of course the Industrial Age. Perhaps by no small coincidence, the field of modern statistics also was born around the same time – roughly 300 hundred years ago. In medicine, an average representing an aggregate population would allow one to scale and manufacture therapies for everyone. For this reason, virtually all clinical trials for therapies including drugs and medical devices, are still analyzed on aggregate populations.

However, the paradigm of Mr. Average has had enormous clinical (as well as social and behavioral) consequences for humans who are outliers. If the population contains a high degree of individual variation, then any average number that is close, but maybe not close enough to be clinically useful to any given individual, is obviously a problem. For this reason a high degree of individual variation poses a serious problem for the healthcare industry.

For example, discovering and developing custom-made pharmaceuticals targeted to a single individual’s biochemistry and that person’s particular variation of a disease is not as simple as

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producing a well-fitted pair of pants. One would first have to measure and decipher the relevant biochemistry underlying the disease variation of that individual and then (if a well-fitted treatment is by coincidence not available) discover, develop, and monitor a custom drug in years of clinical trials (oh, and then be able to charge a few hundred million dollars per individual to recoup at least some of the clinical development costs).

Since we have not and are not able to develop individualized medicines, how bad is it really if we develop them instead for Mr. or Ms. Average - as in fact medical companies currently do? How many people are average? And for those who are not average, will those medicines work?

Fortunately, data on this exact question already exist and the results are astounding - not in a good way. Let’s look at the population performance of the top drugs in migraine, a classic example of a chronic disease with unpredictable but often devastating episodic attacks.

What percentage of the population is effectively treated if you give them the drug in question?

What is astounding is that the best of the acute treatments is ibuprofen, but effective in only 1 in 3 patients. The best preventive treatment in chronic

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### Examples of top drugs marketed or in development in migraine and the portion of the population in which they are effective

<table>
<thead>
<tr>
<th>Migraine prevention (a)</th>
<th>Migraine acute treatment (b)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Chronic migraine</strong></td>
<td><strong>Oral sumatriptan 50 mg</strong></td>
</tr>
<tr>
<td><strong>Topiramate 100 mg</strong></td>
<td>1 in 4</td>
</tr>
<tr>
<td></td>
<td><strong>Oral ibuprofen 400 mg</strong></td>
</tr>
<tr>
<td></td>
<td>1 in 9</td>
</tr>
<tr>
<td><strong>Episodic migraine</strong></td>
<td><strong>Oral aspirin 900 / 1000 mg</strong></td>
</tr>
<tr>
<td><strong>Topiramate 100 mg</strong></td>
<td>1 in 5</td>
</tr>
<tr>
<td></td>
<td>1 in 5</td>
</tr>
<tr>
<td><strong>Erenumab 140 mg</strong></td>
<td><strong>Oral aspirin 900 / 1000 mg</strong></td>
</tr>
<tr>
<td>1 in 6</td>
<td>1 in 5</td>
</tr>
<tr>
<td><strong>Botox</strong></td>
<td><strong>Oral ibuprofen 400 mg</strong></td>
</tr>
<tr>
<td>1 in 9</td>
<td>1 in 3</td>
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<tr>
<td><strong>Erenumab 140 mg</strong></td>
<td><strong>Oral aspirin 900 / 1000 mg</strong></td>
</tr>
<tr>
<td>1 in 6</td>
<td>1 in 5</td>
</tr>
</tbody>
</table>

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**Footnotes**

(a) 50% responder rate; Vo P. et al. Cephalalgia 2017, Vol. 37(1S) 319–374
(b) Diener HC et al. Cephalalgia. 2007 Jul;27(7):814-23
(h) Headache relief at 2 hrs
migraine is topiramate but effective in only 1 in 4. Even more surprising is that Botox, one of the most commonly sought after treatments for chronic migraine prevention is effective in only 1 in 9 patients.

How can this even be possible? The answer is that the efficacy numbers shown in the diagram do not include placebo effect. In real world drug use, the placebo effect can account for 20 to 50% of the response to treatment in patients (about 50% in migraine clinical trials). So placebo effect added to a mediocre but real drug effect equals more acceptable apparent results.

To be sure, nobody is against placebo effect - it is a very safe way to get real clinical benefits. But to answer our question: how effective is it really if we develop medicines for Mr. or Ms. Average? Not very.

The fact that any given drug is therapeutically effective in only a minority of patients flags a number of issues. First, how much faith can we place in any “one size fits all” therapeutic approach? Since the biochemical basis for this failure is poorly understood, shouldn’t we try to understand the mechanisms of individual disease variation that limit the “one-size-fits-all” approach? Finally, and most importantly, how can we develop better therapeutic approaches that are built upon recognition of individual variability?

Migraine, one of the leading causes of disability worldwide, is a model condition if we want to study variation between individuals and the therapeutic implications of these differences. The hallmark of migraine is episodic, debilitating attacks that are easily diagnosed and monitored. In addition, many people with migraine have several attacks per month, so profiling risk factors both positive and negative (e.g. therapies, protectors, potential triggers etc.) associated with making an individual patient better or worse can be done relatively rapidly.

More importantly, patient susceptibility and response to a wide range of potential factors represent an important spectrum of real-world markers for studying individual variation in genetic, physiological, psychological, and ultimately biochemical domains. In addition, many migraine population studies have already been done, generating aggregate data about the average migraine patient, which we can use to benchmark against variation in the individual patient.

A first step toward understanding the level and basis of individual variation in a chronic disease such as migraine versus an “average profile” was recently accomplished in a study done in collaboration with the Department of Neurology, Medical University of Vienna and the

Plot showing mean cycle day of minimum estrogen level in the cycle was day 2 (striped line) but variation in day of minimum estrogen level (range and median day) is shown for each women over three cycles (solid purple line) showing that few women had cycles in which the lowest estrogen day was the same as the calculated mean.
Biostatistics Unit, Faculty of Medicine, Universitat Autonoma de Barcelona, and a healthcare startup called Curelator Inc.

This study, published in *Cephalalgia*, the journal of the International Headache Society, examined risk profiles of more than 300 individual patients. A key aspect of this research was that it examined a previously analyzed database from a landmark study called the PAMINA study where individuals recorded their daily exposure (or lack thereof) to a list of commonly believed “risk factors” (e.g. commonly called “triggers” but also includes non-causal risk factors such as symptoms that might precede attacks or be part of an attack, e.g. neck pain) associated with migraine: weather, dietary, emotional, physical, etc. The original PAMINA study looked at the aggregate population, which yielded the most common trigger associations in that population, namely the “average trigger profile” of the average migraineur. In contrast, the new *Cephalalgia* study reanalyzed the PAMINA database but did so in each of the individual patients. This individualized approach revealed two unexpected findings.

First, virtually all of the patients in the study where a trigger profile was generated showed unique profiles. How many shared an average profile of four potential triggers -- the most common being menstruation, neck pain, tiredness, and bright lights? Not even one patient.

Second, the data revealed that trigger factors in some people were protective factors in others, and vice-versa. To be clear: trigger factors are associated with increasing the risk of migraine while protective factors are associated with decreasing risk of migraine. Why is this an alarming result? Because it is one thing to say: there are factors, possibly including therapeutics, that work in some but don’t work in others. It is entirely another thing to say: this works in some but possibly causes harm in others.

The appearance of “protectors” in individual patients is a significant observation. In chronic diseases such as migraine, protectors - factors associated with decreased risk of an attack - have been observed but never measured before. Why not? One explanation is that the aggregation of patient data is subject to a phenomena called, “Simpson’s paradox”, which concerns the loss of individual signal after population data aggregation occurs, especially in disease populations with high individual diversity. As an example of Simpson’s paradox, if 10 individuals are each sensitive to 10 different protectors, and furthermore, those protectors are triggers in other individuals, then the protector signal will likely be lost after data aggregation.

If we proceed in this manner, the journey started last century to discover individual variation may finally acquire a sense of urgency.
The variation between individual migraine risk factor profiles certainly alerts us that everybody is different on a risk susceptibility level, but will we ever be able to understand the mechanisms driving these differences and relate them to individual therapeutic response?

One of the best studied examples of risk factors for migraine is menstruation and fortunately, data on therapeutic response are also available. As a primary mechanism is believed to be the perimenstrual estrogen ‘withdrawal,’ an effective treatment is application of estrogen gel to ‘bridge’ this deficiency. In a study\textsuperscript{10} of 27 women, the authors chose to apply gel perimenstrually for 7 days ending on day 2 of the cycle – which was median day for lowest estrogen level (nadir) recorded in pre-treatment cycles. However, such was the inter- and intra-individual variation among the women that treating until the median day was inadequate - estrogen was consistently lowest at day 2 in only 5 of 27 women. While estrogen treatment was indeed effective in those five women, women with a later estrogen nadir experienced a delayed estrogen withdrawal migraine, that may not have occurred had the timing of treatment been individualized.

Therefore, it seems that an important next step would be to acknowledge the need to understand both the degree of, and basis for, individual variation in chronic disease. If we proceed in this manner, the journey started last century to discover individual variation may finally acquire a sense of urgency. And if the average approach is limiting, or possibly even causing harm in some individuals – something which might not be detected through aggregate population analysis - then optimizing individual therapeutic pathways and outcomes may be the most effective way forward for patients with chronic disease not adequately addressed by the aggregate approach in modern medicine. \textsuperscript{HW}

References

Your Contributions to the National Headache Foundation Help Fund Projects

What’s being done to help your headache problem? There is an unprecedented amount of research being undertaken regarding migraine and other headache pain. The National Headache Foundation is involved in this effort with the help of funding from you. Contributions are a key part of the financial support of important headache research. Your gift provides funds for (a) NHF-financed research projects, (b) advocacy with health policy decision makers, and (c) patient-education initiatives. You can help! The National Headache Foundation, the #1 source for headache help, provides these services and many others through the generosity of people like you.

Please select one of the following giving categories:

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Migraine disorders affect approximately 37 million people in the United States, and is the most common cause of disability among all neurologic disorders. Nearly 20% of working age females are affected by migraine. And some estimates indicate that migraine and migraine variants cause greater than $22 billion in health costs, missed work, and lost work productivity. Three out of four families in the US are impacted by migraine disorders. Regrettably, more than half of all migraine sufferers who have been treated with migraine prophylactic medications are, or were, dissatisfied with their treatment. And a recent review of medical claims data indicated that as many as 90% of all prescription medications prescribed in the US for migraine prevention are no longer being filled one year later. Clearly, migraine is not a trivial medical disorder and despite advances over the last 2 to 3 decades, there remains unacceptable levels of unmet medical need.

On the positive side, research over the last 15 to 20 years into the role of a brain protein called Calcitonin Gene-Related Peptide (CGRP) in the production of migraine, has focused on one of the primary components of the inflammation and disruption of normal pain processing in the brain that causes migraine disability. Researchers confirmed that CGRP levels increase in the blood stream during migraine. Also, that CGRP administered to patients with migraine causes typical migraine pain and other symptoms to occur. Subsequently, it has been clearly shown that blocking the effects of CGRP can interrupt an ongoing migraine and

Newly Approved CGRP Blocker, Aimovig™ (erenumab) – The First Ever Migraine-Specific Preventive Medication

Timothy R. Smith, MD, R.Ph., FACP, AQH
Study Metrix Research
Saint Peters, MO
can also prevent migraine from occurring in the first place. This finding has led to the development and investigation of possible new medications that target CGRP in migraine attacks. In May, 2018, erenumab, the first of these new medications was approved by the FDA and is now marketed under the brand name of Aimovig™.

Erenumab is a fully human monoclonal antibody which works against CGRP molecules and is produced in laboratories and may be self-administered by migraine patients as a once-a-month injection to prevent migraine attacks before they start. It has its effect by binding to molecules of CGRP in the body and preventing them from reaching their targets, thereby interfering with the process of the underlying migraine mechanism. The clinical trials have shown robust reductions in the number of migraine days, decreases in migraine severity, and improvements in quality of life across populations of patients who routinely experience migraine attacks. This medication action appears to persist over time without losing its effectiveness. And, the overall safety performance is excellent, demonstrating high levels of tolerability in thousands of subjects who received the antibody in the research programs. It is also encouraging to many patients that there are a number of other new novel treatments making their way to the market over the next 2 to 3 years that hold a lot of promise as well, including three other CGRP antibodies (eptinezumab, fremanezumab, galcanezumab), in the same class with erenumab. Clearly, these are exciting times for patients with migraine, their families, and their health care practitioners.

Concern has been expressed over patient access issues as they pertain to erenumab and other new treatments soon to be marketed for migraine prevention, due to expense, coverage, and availability. The National Headache Foundation (NHF), the nation’s premier patient organization since 1970, seeks to deliver on its mission to rid the world of disabling headache disorders by continually executing on patient centric education, research, and advocacy programming. We have recently been conducting opinion surveys with our thousands of patient constituents regarding access to care. One such survey indicated that the most impacted population of migraine patients have experienced significant impediments to new treatments due to cost, coverage, or availability. These patients are eight times more likely to have been denied access to one or more treatments. Additionally, they are twice as likely to be very dissatisfied with their care and management. Ironically, this is the population of patients that the prior approval processes employed by insurance companies should be serving. Yet,
payment/coverage denials persist in this highly impacted group.

The makers/marketers of Aimovig™, Amgen and Novartis, have launched a patient assistance program, Aimovig Ally™, which is designed to help patients and providers navigate the prior approval process. Components to this program could keep the cost of Aimovig™ as low as $5 per month for qualified patients. The NHF applauds this effort and has great hopes that in the coming months and years, with the availability of Aimovig™ and other new treatments for migraine management, we will see unprecedented relief for those most impacted by migraine and other disabling headache disorders. HW

The National Headache Foundation wishes to thank the members of our Corporate Leadership Council for their continued support of the NHF and its mission.

**Diamond Level**
Amgen/Novartis

**Emerald Level**
Eli Lilly and Company

**Ruby Level**
Teva Pharmaceuticals

**Opal Level**
Allergan, Inc.

**Pearl Level**
Alder Biopharmaceuticals
Promius Pharma LLC
Charitable Giving

There are different ways that individuals can support the mission of the National Headache Foundation through donations. A present donation of money or other items of value is the most frequent manner of support. Provisions for specific bequests or residual bequests in one’s will or trust are often utilized. As part of one’s estate planning or planned giving, an individual can provide for charitable giving that may minimize gift and estate taxes while providing for (a) the smooth transfer of ownership, (b) the care and support of dependents, and (c) the avoidance of disputes among survivors.

Three commonly used planned giving vehicles are:

1. **Charitable remainder annuity trust.** Assets (generally securities) are transferred to a trust. The trust makes fixed annual payments to the donor or other specified beneficiaries named by the donor. When the trust terminates upon the death of the donor or other specified beneficiaries, the remainder of the assets in the trust pass to the charity. A trust document is required. The donor retains the ability to change the designated charity.

2. **Charitable remainder unitrust.** Assets are transferred to a trust. The donor or other specified beneficiaries named by the donor receive fluctuating payouts from the trust (a percentage of the value of the principal) and, upon the death of the donor or other specified beneficiaries, the remainder of the assets passes to the designated charity. A trust document is required. The donor retains the ability to change designated charity.

3. **Charitable gift annuity.** The donor, under a contract with a charity, transfers cash or securities to the charity. The charity pays the designated beneficiary a fixed income for life. Upon the death of the beneficiary, the remaining balance passes to the charity. No trust document is required and the charity cannot be changed.
Board Changes

On September 1, 2017, Robert S. Kunkel, MD who served as President of the Board from 1994 to 2005, was named a Director Emeritus by Seymour Diamond, MD, Executive Chairman and Founder.

Three new members joined the National Headache Foundation Board in October, 2017: James W. Banks, III, MD; Katherine Allen Kessler, Esq; and, Tad Seifert, MD. We are sad to report that Doctor James Banks passed away on July 18, while we were preparing to go to press. We will include Dr. Banks' obituary in the next issue.

Katherine Allen Kessler, Esq. is a Managing Director and Associate General Counsel at Citigroup Inc. in New York City. Prior to joining Citigroup in 2004, Katie was an attorney in the litigation departments at Morgan, Lewis & Bockius and Latham & Watkins. Katie grew up in New York City and attended the Fieldston School. She has a BA from Emory University, Atlanta, GA, and a JD from Duke University School of Law, Durham, NC.

Tad Seifert, MD is Director of Norton Healthcare's Sports Neurology Program in Louisville, Kentucky. He is a graduate of the University of Oklahoma College of Medicine in Oklahoma City, Oklahoma. He completed his residency in neurology at the University of Texas-Houston and a subsequent fellowship in headache & facial pain at the renowned Houston Headache Clinic. Dr. Seifert is an Independent Neurotrauma Consultant for the National Football League, and serves as Head of the NCAA's Headache Task Force. He is currently the Team Neurologist for a number of Kentucky and Indiana-based colleges and universities and is Chairman of the Kentucky Boxing & Wrestling Commission's Medical Advisory Panel. His research interests include post-traumatic headache in athletes as well as combat sports medicine.

Two members, Josh Friedman, Esq. and Alan Rosenberg, MD, resigned from the Board during 2018. We wish to thank them for their support and counsel during their tenure on the Board.

LECTURESHIPS

On an annual basis, the NHF awards two lectureships to recognize achievement in headache medicine. This year, the lectures were presented at the Diamond Headache Clinic Research & Educational Foundation 32nd Annual The Practicing Physician's Approach to the Difficult Headache Patient, which was held at the La Costa Resort and Spa, Carlsbad, CA, from February 16 through 18, 2018.

The Seymour Diamond, M.D. Lectureship

Annually, in honor of the National Headache Foundation's Executive Chairperson and one of its founders, the Foundation presents the Seymour Diamond, M.D. Lectureship Award which recognizes the most significant paper in headache published during the past year. This year's recipient was Timothy T. Houle, Ph.D.

Doctor Houle is Associate Professor of Anesthesiology at Harvard Medical School/Massachusetts General Hospital, Boston, Massachusetts. He previously served as Associate Professor on Anesthesiology and Neurology, at Wake Forest School of Medicine in Winston-Salem, NC, and as Adjunct Research Assistant Professor of Physical Medicine and Rehabilitation at Northwestern University, Chicago, IL.

He received his BA in Psychology (Magna Cum Laude), from the University of Wisconsin – Milwaukee, and PhD in Clinical Psychology, at the Illinois Institute of Technology, Chicago, IL. Doctor Houle completed a Postdoctoral Residency in Clinical Psychology at the University of Mississippi Medical Center in Jackson, MS. He completed a Postdoctoral Fellowship in Pain Psychology at the Rehabilitation Institute of Chicago.

Dr. Houle is a member of the American Headache Society, and served as the Chair of its Research Methods Section from 2013 through 2015. He is a member of the American Society of Anesthesiologists and the Southern Headache Society.
Dr. Houle serves as an Ad Hoc Reviewer for several professional journals, including the Clinical Journal of Pain, European Journal of Pain, JAMA, and Pain. He is the Statistical Consultant for the journal, Headache, and is an Associate Editor of Cephalalgia. His research investigations have resulted in over 110 articles in peer-reviewed journals.

Dr. Houle's lecture, “Forecasting Individual Headache Attacks Using Perceived Stress: Development of a Multivariable Prediction Model for Persons with Episodic Migraine” was based on an article of the same title which appeared in the journal, Headache 2017; 57:1041-1050. His coauthors were: DP Turner, AN Golding, JAH Porter, VT Martin, DB Penzien, and CH Tegeler.

The National Headache Foundation Lectureship

The NHF created the National Headache Foundation Lectureship Award to preserve the highest level of neurobiological research and advancement in medicine today. Recipients of the award prove themselves to be up-and-coming physicians and scientists who have demonstrated interest in the management of common and complex headache problems. In addition, the honorees have impressive research experience as evidenced by the poster presentations and published articles which have been reviewed by the Award Committee. This committee is comprised of physician members of the NHF Board of Directors and the Honorary Board. The Lectureship is presented annually at a scientific meeting. The 2018 recipient of The National Headache Foundation Lectureship is Mia T. Minen, M.D., M.P.H.

Doctor Minen is Chief of Headache Research, Division of Headache Medicine, at New York University Langone Medical Center, in New York City, where she previously served as Director of Headache Services. She is also an Assistant Professor, Department of Neurology at New York University Langone Medical Center. She completed a Headache Medicine Fellowship at the Graham Headache Center at Brigham and Women’s Faulkner Hospital, Boston, MA, and a Neuropsychiatry and Behavioral Neurology Fellowship, at Massachusetts General Hospital, Boston, MA.

She received her Bachelor of Arts degree in psychology, magna cum laude from Barnard College, Columbia University in New York, NY, and a Master of Public Health in Epidemiology, from the Mailman College of Public Health at Columbia University. She received her M.D. at Jefferson Medical College in Philadelphia, PA. She completed an internship at St. Luke’s – Roosevelt Hospital, New York City, and a residency in neurology at Columbia Presbyterian Medical Center, in New York City.

She is a Diplomate of the American Board of Psychiatry and Neurology. In 2014, Dr. Minen received the subspecialty certification in Headache Medicine as well as subspecialty certification in Behavioral Neurology-Neuropsychiatry from the United Council for Neurologic Specialties. She is a member of the American Academy of Neurology, and a Fellow of the American Headache Society.

Doctor Minen has received numerous honors, including the American Headache Society’s Frontiers in Headache Research Award (2014), American Academy of Neurology Institute Fellows Scholarship (2014), and was an International Headache Academy Grant Awardee (2014-2015). She was named to the American Academy of Neurology’s Emerging Leaders Forum Program (2014-2015) and Palatucci Advocacy Leadership Forum (2013). In 2016-2018, she was the recipient of the American Academy of Neurology/American Brain Foundation Practice Research Training Fellowship.

She has published over 30 research papers, presented numerous oral presentations on headache, and serves as an Associate Editor for Headache. Dr. Minen is a member of the Editorial Board of Pain Medicine, and serves as a Reviewer for the journals, Cephalalgia, Journal of Headache and Pain, and BMC Public Health. Dr. Minen is a Member of the American Academy of Neurology Guideline Development, Dissemination, and Implementation Committee; Chair of the American Headache Society Emergency, Inpatient, and Refractory Section; and, is a Member of the International Headache Society and the Research Committee of the American Neurologic and Psychiatric Association.
Certificate of Added Qualification in Headache Medicine

The following healthcare practitioners have received the Certificate in Added Qualification during the past year:

**March, 2017:**
- Martha Aregbesola, NP Wisconsin
- Karen Mae Bontia, MD Texas
- Sau Mui Chan-Goh, ARNP Washington
- Akram Dastagir, MD Wisconsin
- Misty Doering, APRN Connecticut
- Deanna Duggan, CPNP Texas
- Luis Figueroa, MD Florida
- Miguel Figueroa, MD Florida
- Sara Freeman, PA Texas
- Alana Harrison, APRN Virginia
- Michelle Holick, MD Texas
- M Barrett Horton, NP Texas
- Abdel Salam Kaleel, MD Ontario, Canada
- Brooke Madden, MD Oregon

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<th>Name</th>
<th>Specialty</th>
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<tr>
<td>Carol Matthews</td>
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<td>Pedram Navab</td>
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<td>Tara Pezzuto</td>
<td>APRN</td>
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<td>Brian Sorin</td>
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<td>Peter Joseph Struck</td>
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<td>Arash Taavoni</td>
<td>DO</td>
<td>Maryland</td>
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<tr>
<td>Elaine Timm</td>
<td>MD</td>
<td>Texas</td>
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**September, 2017:**
- Diane Ryder Counce, MD Alabama
- Amy Dix, PA-C Kansas
- Amr Hosney, MD New Jersey
- Jeffrey Kaplan, MD Kansas
- Seth Lichtenstein, MD Pennsylvania
- Alla Mesh, MD New York

**March, 2018:**
- Noman Ahmed, MD Wisconsin
- Katherine Brown, PA-C Georgia
- Emily C. Johnson, MD Michigan
- Amy Jones, NP Kentucky
- Rosamma Joseph, MD New York
- Kate Kennedy, NP Washington
- Ashley E. Knable, NP Indiana
- Richelle de Mayo, MD Connecticut
- Denise M. McGrath, NP Connecticut
- Gretchen T. Michaelson, NP Connecticut
- Brooke Phenicie, NP Illinois
- Melissa K. Ramsdell, NP Virginia
- Mai Mona Rasoully, NP New York
- Sarah G. Waddell, NP Virginia

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Thank you to our Diamond Level Sponsor: **Lilly**
The NHF hosted the 32nd Annual Fundraising Benefit – *Casino Royale - Betting on a Cure for Headache*, on May 5, 2018, at the Ritz-Carlton Chicago. Guests enjoyed the dinner and dancing to the Don Cagen Orchestra. The event also included a raffle, silent auction, Wall-of-Wine, and Fund-A-Need. Two awards were presented during the evening.

**Partners in Excellence Award:**

Doctor Julian E. Bailes is the Chairman of the Department of Neurosurgery at the NorthShore University HealthSystem and Co-Director of the NorthShore Neurological Institute, Evanston, IL. He is also a former NFL and current NCAA team physician. Dr. Bailes has dedicated his career to the study of traumatic brain injuries, chronic traumatic encephalopathy (CTE), and associated post-traumatic/post-concussive headaches.

Dr. Bailes received his M.D. from the Louisiana State University School of Medicine in New Orleans. His internship and residency in neurosurgery were completed at McGaw Medical Center of Northwestern University, Chicago, IL. He completed a Fellowship at Barrow Neurological Institute, Phoenix, AZ.

In 2005, Dr. Bailes contacted Dr. Bennet Omalu, the pathologist who discovered a disease he named “chronic traumatic encephalopathy” in the brains of deceased football players. It was a turning point in Dr. Omalu’s effort to get the NFL — and the world — to recognize a link between repeated blows to the head and telltale changes in the brain associated with depression, early-onset dementia, aggressive behavior, and suicide. At the time, Dr. Bailes was medical director of the Center for the Study of Retired Athletes at the University of North Carolina, and he had been a team doctor for the Pittsburgh Steelers. Joined by a cadre of physicians, attorneys and public health specialists, they forced a reluctant NFL to take some responsibility for the safety and brain health of its players. Their story is recounted in the 2015 film, *Concussion*, and Dr. Bailes is portrayed by Alec Baldwin.

**Lifetime Achievement Award of the National Headache Foundation:**

Vincent T. Martin, M.D.

Vincent Martin, M.D. is the Director of the Headache and Facial Pain Center at the University of Cincinnati Gardner Neuroscience Institute, and has been a Professor of Clinical Medicine in the Division of Internal Medicine since 2004. Dr. Martin is the President of the Ohio Headache Association and President of the National Headache Foundation.

After graduating from the University of Dayton, he received his M.D. from the University of Cincinnati College of Medicine. Dr. Martin completed a residency in internal medicine at the University of Cincinnati, followed by a fellowship in general internal medicine there, at UC. He is board certified by the American Board of Internal Medicine, board certified in Headache Medicine by the United Council for Neurologic Subspecialties, and is a Diplomat of the National Board for the Certification of Headache Experts. In 2002, he received the Certificate of Added Qualification in Headache Medicine (CAQ) from the NHF. Doctor Martin is a Fellow of the American College of Physicians and a Fellow of the American Headache Society. He serves as a reviewer for the *Journal of Family Practice* and the *European Journal of Neurology*. Doctor Martin is an Associate Editor for the journal, *Headache*. He is a Board member of the Alliance for Headache Disorders Advocacy and attends the annual, *Headache on the Hill*. He has written over 60 articles for the professional literature and contributed 10 chapters to various headache textbooks. In addition, Dr. Martin has conducted many studies on headache.
The Baylor Scott & White Headache Clinic was established in August, 2008. The Neurology department chair, Richard Lenehan, MD, invited D. Michael Ready, MD, to transfer from the Family Medicine department to the Neurology department to start a dedicated headache clinic.

The following is based on interviews with the medical staff of the clinic. The Director of the Clinic is Cristina Cabret-Aymat, MD. Dr. Cabret-Aymat attended medical school at the University of Puerto School of Medicine, Río Piedras, PR. She completed her neurology residency at Boston University Medical Center, and a Headache Fellowship at the University of Southern Florida, Tampa, FL. Dr. Cabret-Aymat is board certified in neurology, and has received subspecialty certification in headache medicine from the United Council of Neurologic Subspecialties.

D. Michael Ready, MD, served as Director of the Clinic from its inception in August, 2008, through June, 2016. Dr. Ready attended Texas Tech University School of Medicine, Lubbock, TX. He completed a residency at Brazos Valley Family Medicine, part of Texas A&M University Medicine in Bryan, TX. Dr. Ready is board certified in Family Medicine, and has received subspecialty certification in headache medicine from the United Council of Neurologic Subspecialties.

Linda Kirby-Keyser, MD, graduated from the University of Texas Medical Branch, Galveston, TX. She completed her residency in Pediatrics at the University of Iowa, Iowa City, IA. Dr. Kirby-Keyser is board certified in Pediatrics, and has received subspecialty certification in headache medicine from the United Council of Neurologic Subspecialties. Jennifer Padilla, MD, attended Universidad Central del Caribe, Bayamon, Puerto Rico. Doctor Padilla completed a residency in neurology at the University of Texas, Houston, TX, and a fellowship in headache medicine at the University of Miami, Miami, FL. She is board certified in neurology from the American Board of Psychiatry and Neurology.

Most of the patients are typically referred by health care providers (both internal and those not practicing within the Baylor Scott & White system), although a patient
may schedule an appointment without a referral, if their evaluation is allowed by their insurance carrier. Patients of all ages are seen at the Clinic. Children are evaluated by Drs. Kirby-Keyser or Dr. Ready. As in most headache specialty centers, the majority of patients are experiencing migraine. However, patients with all types of headaches are examined, including those with cluster headache, hemicrania continua, new daily persistent headache, most common neuralgias such as trigeminal, and post-traumatic headache. For those patients presenting with a secondary headache disorder, the staff attempt to identify the underlying condition and determine the most appropriate intervention(s) needed to achieve a satisfactory resolution of the headache.

Almost all of the patients will attend a “headache class” prior to their examination at the clinic. At the time of the class, a headache intake form is provided and that form will serve as a starting point for the initial visit. During the initial visit, a headache history is obtained and a physical examination is performed. Once the diagnosis is established, it is discussed with the patient, a treatment plan is agreed upon, and a follow-up appointment is scheduled. A typical day at the Clinic involves four new patient evaluations and at least eight follow-up visits. Certain days of the week are dedicated to procedures, such as onabotulinum toxinA injections for chronic migraine prevention. Some appointment times are reserved for urgent needs such as rescue medications.

Biofeedback is provided at the Clinic as Dr. Kirby-Keyser is a certified biofeedback practitioner. If deemed appropriate, patients are admitted to the neurology department at the hospital. Typically, the patients will receive during the admission, multiple intravenous, procedural, physical, and psychological interventions in order to maximize the benefits of an inpatient stay and improve the headaches.

When asked about the existence of a particular treatment philosophy at the Clinic, the staff concurred that they believe that the most effective headache care is provided through a collaborative relationship between the clinician and the patients. This relationship requires that the patients learn about their disease. The goal for the patient should be to learn enough about their headache disorder so that they may direct their headache physicians to manage the needed treatment. They have found that a patient does best when they are close to their primary care provider. As a result, patients are discouraged from traveling great distances to the Headache Clinic.

The addition of Dr. Padilla as the fourth headache specialist decreased wait times for appointments for headache clinic referrals. They are seeking a partner for their “sister” clinics within the Baylor Scott & White system in order to improve headache care.

When asked why she chose headache medicine, the Clinic director, Dr. Cabret-Aymat stated: “I became interested in headache medicine as a neurology resident while working with my attending at the time, Dr. Brian McGeeney. Migraine patients presented to clinic and hospital with their whole lives disrupted, feeling ignored and misunderstood most of the time because a lot of them felt very few people truly understood the scope of migraine disease. I went to my first headache meeting in Stowe, VT, at the Headache Cooperative of New England Symposium, and as I sat there listening to headaches...
cases, I knew this is what I wanted to do. Along with proper diagnosis, education of the condition, medication, and lifestyle changes, patients become better. In our field, we make an important and positive impact in patient’s qualities of life and help them take control of their lives.”

Dr. Ready, who served as Director from August, 2008, through June, 2016, stated that he went into headache medicine because: “I became interested in headache medicine soon after starting at Scott & White. I realized that I had not been prepared to manage headaches effectively by my residency training. I started attending headache meetings, such as those offered by the Diamond Headache Clinic Research & Educational Foundation, and I soon realized why my patients were not getting better. I had not been providing appropriate care. I noticed that my migraine patients were different than my other patients in family medicine in that they would do almost anything that I had asked them to do as long as it would make the headache go away. I still remember the first patient to whom I provided a subcutaneous injection of sumatriptan. Following the injection, I left her alone in a dark room for 10 minutes. Upon returning, I asked her how the headache was. She arose from the examination table where she had been lying down, and had a confused and surprised look on her face. She started looking around the room as if to observe the demon that had been tormenting her. She said, ‘I know it is around here somewhere but I don’t feel the migraine any more.’ I thought to myself, this is why I became a physician. Rarely, do you have the opportunity to have such a dramatic effect in someone’s life. Most everyone with migraine wants the same thing – they want their life back. We want to help them get it.”

When asked what they enjoy most about working in headache medicine, the physicians concurred that: “It is the patients and our colleagues. In our clinic, we truly enjoy the people who trust their headache care to us. The best part of our day are patients letting us know that they are better and that they were able to do something that in the past, a headache would not have allowed them to do. Our community of headache specialists is a great one to be part of as well, and we are thankful we get to work with such a great group of people every day.”

For patients experiencing headaches, the staff offered this advice: “Learn as much as possible about your condition so that you can be a better partner in care.”

FOR MORE INFORMATION ON THE CLINIC, PLEASE VISIT:

www.bswhealth.com/locations/temple-clinic/
The Baylor Scott & White Headache Clinic
2401 South 31st Street
Temple, TX 76508
(254) 724-4179 or (800) 792-3368
Hours: Monday - Friday
8 a.m. - 5 p.m.
NHF suggests answering the following questions to compile your headache history:

- When did you start having headaches?
- How often do they occur? At what time of day? During the week or on weekends? How long do they last?
- Where is the pain?
- Which word best describes it: throbbing, pounding, splitting, stabbing, and blinding?
- Are your headaches associated with your menstrual cycle?
- What triggers your headache: certain foods, certain physical activities, bright light, strong odors, change in temperature or altitude, noise, smoke, stress, and oversleeping?
- What symptoms do you experience prior to the headache?
- Does anyone else in your family suffer from headaches?
- Do you notice visual disturbances before or after your headaches?
- Do you suffer from more than one type of headache?

It is important to make an appointment with your doctor for the specific purpose of addressing your headache history rather than discussing headaches as part of a physician visit for other reasons. The National Headache Foundation also recommends keeping a diary to track the characteristics of your headaches. Patterns identified from your diary may help your doctor determine which type of headache you have and the most beneficial treatments.

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<th>Date</th>
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<th>Intensity (rate 1-10, most severe being 10)</th>
<th>Preceding Symptoms</th>
<th>Triggers</th>
<th>Medication (and dosage)</th>
<th>Relief (complete/moderate/none)</th>
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For more information about headache causes and treatments, visit the NHF web site at: www.headaches.org or call 888-NHF-5552

820 N. Orleans, Suite 201, Chicago, IL 60610-3132
Toll Free (888) NHF-5552 Fax (312) 640-9049
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