President’s Message
Deborah Carver Hodges, MD

As physicians, we are not typically political or business minded. Over the past several years there has been a growing frustration with both the political and business issues that we as physicians and our patients have been experiencing. I have heard from some of you about your frustration over the MOC, EMR, MARCA or the fact that it is harder and harder to get medications, even generics, approved that our patients need.

For that reason, the Texas Neurological Society hired and continues to employ our own Lobbyist, Greg Herzog, to serve as an advocate for our needs at the state level. For the business aspect, Kristi Berrier, is here to help us as our own medical economic advisor.

However, a wise women (my mom) always liked to tell me, ‘if you don’t tell people what is wrong, it will never be corrected’. So I would encourage you to reach out to your local congressman/woman. Also, consider joining other physicians at First Tuesday. This year the dates are February 2, March 7, April 4 and May 2. The Neurology day is scheduled for April 4th. For those who are interested in participating in any of those dates, there is a $500 stipend that covers travel for those who attend if you contact Ky at Ky.camero@texmed.org.

Also please encourage your patients who have insurance or medication hassles/ issues to send their complaints to Texas Department of Insurance. @ http://www.tdi.texas.gov/consumer/complfrm.html

Now on a lighter note: I am looking forward to seeing every one at the Winter Conference February 24-26, 2017 at the Hyatt Regency in Austin. The Hyatt has newly redone conference space and Dr. Eddie Patton, program director, has an excellent line up of speakers and topics. Also please reserve the date in the calendar for the Summer Conference, which is at Lost Pines in Bastrop Texas, July 28-29, 2017. Dr. Gina Jetter is already working on an impressive lineup of speakers.

It has been an honor to serve as your TNS president this year. However, I could not do it without the support of Ky Camero. She is the one who actually keeps the TNS running smoothly. Please take a moment the next time you see her and thank her for all that she does! Hope you all have a great 2017!
This Issue

I thank our officers and other contributors for their excellent submissions to this issue. We look forward to seeing you at the TNS 20th Annual Winter Conference in Austin, February 24-26. Eddie Patton, program director, Bob Fayle, education committee chair, and the education committee have planned an excellent program.

Thyroid Disease and Headaches

Hypothyroidism can be a cause of headaches and a secondary cause of new daily persistent headache (NDPH) with an unknown mechanism.

About 30% of those with hypothyroidism present with headaches often within 1-2 months of the first symptoms of hypothyroidism. In one prospective study, the headaches were typically bilateral, non-pulsatile, continuous, and of mild intensity (Moreau T, Manseau E, Giroud-Baleydier F, Dumas R, Giroud M. Headache in hypothyroidism. Prevalence and outcome under thyroid hormone therapy. Cephalalgia. 1998;18(10):687-689).

A cross-sectional study found different features similar to migraine (Lima Carvalho MF, de Medeiros JS, Valença MM. Headache in recent onset hypothyroidism: Prevalence, characteristics and outcome after treatment with levothyroxine. Cephalalgia. 2016 Jul 7 [Epub ahead of print]). The headaches could be unilateral or bilateral, pulsatile in 63%, moderate to severe intensity in 72%, associated with nausea/vomiting in 60%, and have a duration of 4-72 hours in 78%. 53% had a history of migraine. After treatment with levothyroxine, 78% reported a decrease in headache frequency with similar benefit in those with both subclinical and hypothyroidism.

In a study of patients with NDPH, hypothyroidism was much more common in those with NDPH as compared to those with migraine and chronic post-traumatic headaches (Bigal ME, Sheftell FD, Rapoport AM, et al.: Chronic daily headache: identification of factors associated with induction and transformation. Headache 2002, 42:575–581).


There are 12 cases reports of thyroid replacement therapy associated with pseudotumor cerebri with a duration of thyroid treatment prior to the diagnosis of PTC of 1-18 weeks (Beal CJ, Pao KY, Hogan RN. Intracranial hypertension due to levothyroxine use. J AAPOS. 2014 Oct;18(5):504-507).

In summary, you should strongly consider obtaining thyroid-stimulating hormone (TSH) and free T4 in patients with new onset frequent headaches or an exacerbation of their migraines.

Ageism And The Invisible Patient

My father passed away almost 2 years ago at the age of 92. In his later years as I would go out with him to stores or physician visits, he became almost invisible. Sales people or physicians would typically talk to me and ignore him assuming he was demented.

Ironically, he retired at the age of 88 as a distinguished university professor of social psychology, behavioral medicine, and health psychology and was cognitively superior his entire life. For decades, he had studied prejudice and discrimination. Father and son, psychologist and neurologist, would discuss his experiencing the effects of ageism which he had studied as a younger person and I would consider my own interactions with patients as I have aged.

Ageism might be the last social bias tolerated where people are treated with preconceived notions of their age by people of all ages. Mark Zuckerberg addressed a gathering of start-ups saying, “Young people are just smarter” (which may be true in his case and a lot richer). Older competent people have a more difficult time finding employment (perhaps with the exception of the president-elect). A common theme of birthday cards is advancing age as a basis for humor. (“Age is important only if you’re cheese or wine.” “I used to get lost in the shuffle; now I just shuffle along with the lost.” “You’re so old you confuse having a clear conscience with having a bad memory.” “I’m on a 30 day diet. So far, I’ve lost 15 days.” “Your supply of brain cells is finally down to a manageable size.” “You know you are old when you’ve been diagnosed with CRS (can’t remember shit).”

In a large nationwide survey, about 20% of those over age 50 reported experiencing discrimination in healthcare settings (Rogers SE, Thrasher AD, Miao Y, et al. Discrimination in Healthcare Settings is Associated with Disability in Older Adults: Health and Retirement Study, 2008-2012. J Gen Intern Med. 2015;30(10):1413-20). They may feel that they get no respect from the healthcare professional or system. Geriatrics is a small and unpopular subspecialty and there is a shortage of education in the healthcare professional or system. Geriatrics is a small and unpopular subspecialty and there is a shortage of education in the healthcare professional or system. Geriatrics is a small and unpopular subspecialty and there is a shortage of education in the healthcare professional or system.

In my own treatment of the elderly, in many cases, their children may dominate the interaction and I may address them rather than their parent. Unfortunately, many of our patients are demented but even then, they appreciate being directly addressed and considered.

So consider the obvious. Interact with older patients as you or your family would desire.
The issue of ‘fail-first’ or ‘Step-Therapy’ has gained interest with legislators. This is the practice by health plans to require your patients to fail on one drug before allowing the drug that you think is best for your patient. While no one disputes that this practice has some cost benefits, the transparency of the process with respect to appeals and procedure is often non-existent. The TNS board believes that your prescription pad should not be turned into a ‘suggestion pad’.

**ABIM AND THE MAINTENANCE OF CERTIFICATION (MOC):**

Nationally, the anger in some physician quarters at the ABIM’s MOC has reached a boiling point. Several states’ legislatures have debated bills like a bill that passed in Oklahoma this year that prohibits licensure boards, health plans, and hospitals from using the MOC as standard for licensure, credentialing, or privileges. We believe that similar language will be offered this session and we will be monitoring it closely.

**OTHER ISSUES OF NOTE:**

Legislation last session legalizing the limited use of non-THC cannabis, or CBD Oil, has hit a roadblock at the agency tasked with regulating the sale of the product. The facility licensure fees levied by the Department of Public Safety are thought to be too excessive to allow any facility entry into the Texas market. The Legislature may act on this topic again.

Technology and the future of telemedicine will be heavily discussed this session with the conversation involving payment for services and what constitutes the proper delivery of care. The Instrastate Compact is one of the components designed to assist those physicians working across state lines. The Compact does not mean that a Texas license is equivalent to another state license. It simply means that Texas will be able to utilize the background information done by other states when evaluating whether to issue a new license.

Two issues that fall into the realm of Hot Button will almost certainly be discussed: In light of high-profile Texas cases, the end-of-life issue debate appears to be set for further discussion. Allowing personal firearms in healthcare facilities and other venues will be heavily discussed by this legislature.

**THE EYE TOWARDS WASHINGTON:**

The nomination of US Representative Tom Price, MD (R-Georgia) as HHS Secretary is the most interesting cabinet pick for physicians because he will be the boss of the CMS director. Since MACRA came out, Republicans have been paying lip service to physicians about how all these rules and regulations promulgated by CMS were not what they intended with the new law, and they blamed the excessive regulations on the Democrats. The Republicans have been talking the talk, now that they are in the majority, they will get a chance to walk the walk. TMA and AAN are actively working to suggest changes to make MACRA easier to deal with. If the Affordable Care Act is appreciated changed, it may carry some changes to Medicare and Medicaid as well and physicians for sure want to be in on that conversation.

**FINALLY:**

As always, your TNS Board of Directors is open to any suggestions or comments. Please consider being an advocate for your patients and your practice. Engage your local elected officials and offer yourself as a resource for them as they consider public policy questions that impact your practice and patients. Consider attending TMA’s First Tuesdays and Neurology Day, April 4th. Stay tuned for more!
President-elect Trump has promised that he will repeal and replace the 6 year old Affordable Care Act (Obamacare); a major legislation that has had an impact on every aspect of U.S. Healthcare. While we do not have many details what dismantling the ACA will be, we do know that as president, Mr. Trump will replace the cabinet secretaries and most of the political appointees in the Departments of Health and Human Resources, Labor, and Treasury; the branches which administer the ACA. In addition, since the ACA is dependent on provisions and other governmental elements working in concert, disrupting the economic interactions of the ACA would lead to serious distortions in the operation of the program in tandem with further disruption in the already tenuous insurance markets and exchanges. But abolishing the ACA will not be accomplished simply by a stroke of the pen. The Affordable Care Act has become such an integral part of the nation’s health care landscape, actual repeal and replacement will require significant and complicated congressional legislation. The biggest issue will be what to do with the 20 million Americans who have gained insurance coverage under the ACA. Thus it is likely that any repeal package would also include a transitional period which would be accompanied by some type of replacement package outlined by companion legislation as a replacement for the ACA. As is well known, the devil is always in the details.

In addition to the repeal and replacement of the Affordable Care Act, the election outcome both for presidency as well as congress, will impact additional important healthcare programs which include Medicare, the administration and payments for Medicaid, new delivery system reforms such as The Medicare Access and Chip Reauthorization Act of 2015 (MACRA), ever rising drug prices, the future of powerful government agencies created under the ACA including the Center for Medicare and Medicaid Innovation (CMMI), and the elimination of the Independent Payment Advisory Board (IPAB) - a key provision of the ACA that large numbers of physicians, physician medical societies and some lawmakers have fought to eliminate since inception. The CMMI is a particularly important government organization which functions under CMS. As established by the ACA, this organization has a $10 billion appropriation every 10 years, into perpetuity. The CMMI has much authority in testing and developing innovative payment and delivery system models that are created to improve quality of care while reducing the cost of care. Such models as medical homes, all-payer payment reform, and arrangements that transition from fee-for-service reimbursements to global fees and salary-based payment are models of reform under the jurisdiction of CMMI. Some CMMI programs are models which can be instituted without requiring congressional approval; others like MACRA do require congressional approval. In addition to eliminating CMMI, repeal of the ACA would also eliminate other government programs such as individual and employer mandates, the medical device tax and the tax on high-cost employer health benefit plans (Cadillac tax). Repeal of the ACA, however, would not eliminate MACRA. While the ACA was passed in 2010 with exactly zero Republican votes, the law was intended to increase health insurance quality and affordability, lower the uninsured rate by expanding insurance coverage, and reduce the costs of health care. MACRA was passed in 2015 and was designed to eliminate the Sustainable Growth Rate formula by establishing a new way to pay doctors who treat Medicare patients. MACRA was passed with a bipartisan vote of 392-37 in the House and 92-8 in the Senate. MACRA is not Obamacare! While some parts of these laws are intertwined, the impact of repeal of the ACA will not eliminate MACRA. While it is anticipated there will be real time alterations and corrections to MACRA, to date, neither Mr. Trump nor the Republicans in congress have made mention of repealing MACRA.

There are obviously many more complex healthcare considerations for the new administration in addition to the repeal of the ACA. A full repeal would not only eliminate the insurance market reforms such as guaranteed issue, but would also affect the ACA’s reimbursement rate cuts to hospitals and other health care providers. Many large healthcare systems nationwide, despite vigorous cost reducing measures including decreased length of stays, are already feeling a significant economic impact as a result of decreased reimbursements. Because of the economic impact on hospitals, there are some healthcare leaders who predict that by 2025 there may only be about 150 major healthcare systems providing the majority of healthcare within the U.S. The Congressional Budget Office (CBO) projects that the Medicare spending will double by year 2026. While these projected statistics are partially driven by our aging population, the most current 2014 statistics indicate that our government already spends $3 trillion for healthcare annually which translates into about $9,523 per person in the U.S. Of the $3 trillion spent on healthcare in 2014 about 1/3 or $971.8 billion are related to hospital costs, $603.7 billion for physician clinical services, and $297.7 billion for retail drug costs. The U.S. healthcare expenditures are currently about 17.5% of our GDP. Obviously these numbers of expenditure for healthcare are unsustainable. Based upon the current numbers, the Medicare Trustees estimate that the Medicare Hospital Insurance trust fund will expire in 2028. In an effort to address these rising healthcare costs, the Ways and Means Finance Committees will continue to explore alternative payment models which will include alternatives to fee-for-service as bundled payments. Bundled payments and alternative payment models are actually a part of the current ACA. Another major emphasis in any post ACA healthcare reform will be Medicare’s efforts to combat fraud and abuse which costs the government and taxpayers billions of dollars per year. The economic concerns of the viability of Medicare were important considerations in the congressional bipartisan implementation of MACRA. Thus, the election’s outcomes potentially impact a range of healthcare issues and new opportunities for healthcare stakeholders.

President-elect Trump promises to “…broaden healthcare access, make healthcare more affordable and improve the quality of the care available to all Americans”. He indicates that our elected representatives in the House and Senate must:
1. Completely repeal Obamacare
2. Modify existing laws that inhibit the sale of health insurance across state lines; thus allowing increased competition within this market
3. Allow individuals to fully deduct health insurance premium payments from their tax returns under the current tax system.
4. Allow individuals to use Health Savings Accounts (HSAs). Contributions into HSAs would be tax-free and should be allowed to accumulate. These accounts would become part of the estate of the individual and could be passed on to heirs without fear of any death penalty. These funds can be used by any member of the family without penalty.
5. Require price transparency from all healthcare providers, especially doctors and healthcare organizations like clinics and hospitals.
6. Block-grant Medicaid to the states. It is felt that the state governments ... can manage the administration of Medicaid far better without federal overhead.
7. Remove barriers to entry into free markets for drug providers that offer safe, reliable, and cheaper products. ... Allowing consumer's access to imported, safe and dependable drugs from overseas will bring better options to consumers.

The above 7 points are referenced from Trump/Pence Make America Great Again; Healthcare Reform to Make America Great Again. https://www.donaldjtrump.com/positions/healthcare-reform.

The 115th Congress will be addressing all of the points discussed above.

To help our members better understand the projected changes in healthcare that will affect all physicians, as well as the newly constructed 17 October 2016 – 2398 page Final Rule on MACRA, the TNS has invited Robert Michael Kropp, MD, MBA, CPHI, to give a special presentation at the 2017 Austin TNS Winter Conference; February 24 – 26. Dr. Kropp is a triple-boarded physician executive and Hopkins-trained informaticist. He is Board Certified in Neurology, Pediatrics and Clinical Neurophysiology. In addition he holds an MBA from the University of South Florida and a Certificate in Public Health Informatics from John Hopkins School of Public Health. Dr. Kropp was the national Senior Medical Director and Vice President of Clinical Transformation for Aetna’s Accountable Care Solutions. As such, he was responsible for the clinical programs that more than 70 ACOs used nationwide to improve quality, efficiency and patient experience. Prior to Aetna, he held a variety of prestigious positions in the managed care industry, including Chief Medical Officer for CIGNA Healthcare of Florida. While in clinical practice, Dr. Kropp also held an academic appointment at the University of South Florida and an administrative appointment as Head of Child Neurology at All Children’s Hospital in St. Petersburg, Florida. Dr. Kropp currently serves on the American Academy of Neurology Medical Economics and Management Board as well as the AAN Payment Alternative Team. He is one of the most highly respected national advisors to the AAN. To better understand the projected future changes in healthcare and how those changes will affect neurologists nationwide, I strongly encourage you all to attend Dr. Kropp’s TNS Medical Economics presentation at the 2017 TNS Winter Conference.

About the Thymectomy Trial in Myasthenia Gravis

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Baylor College of Medicine,
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What was the rationale for the thymectomy trial? For more than 80 years, thymectomy was practiced for patients with MG with no systematic evidence to support it. The practice was based on case reports published by Blalock demonstrating efficacy of thymectomy in a myasthenic patient with thymic tumor and several patients without tumor. Retrospective studies provided conflicting results and many of them were methodologically flawed. It was about time to put this question through a controlled prospective clinical trial.

What was the design of the trial? The trial included patients with seropositive MG (AChR antibody titer of more than one) with at least MGFA class 2 (scale 2-5) whose age ranged between 18 and 65 years. Close to 6000 patients were screened and only 126 patients were included. Patients were randomized to external transsternal thymectomy with alternate day prednisone vs. alternate day prednisone alone. Patients were followed for three years. Patients wore high T-shirts to hide thymectomy scar.

What were the major reasons for not being included in the study? Duration of myasthenia gravis (only less than 5 years duration was accepted), age, use of nonglucocorticoid immunosuppressive drugs, previous thymectomy or chest surgery, and declining to participate.

What were the primary outcome measures? Average Quantitative MG score and average dose of prednisone needed.

Does the trial provide clinical guidelines for the practicing neurologist? Thymectomy patients measured three years later had a better QMG score, needed less steroids, less likely needed azathioprine, had less complications from treatment and less admission to the hospital. The difference was moderate. For the first time, the impact of thymectomy in MG was demonstrated via a clinical trial.

Did the trial prove efficacy of thymectomy in certain age or sex groups? Unfortunately, the population size was not enough to provide a meaningful subgroup analysis.

What were the drawbacks of the trial? The trial was single blinded. It was not ethical to do sham thymectomy.
Cluster Headache: History, Mechanisms, and Most Importantly, Treatment Options for Refractory

Mark J. Burish, MD, PhD
Director, Will Erwin Headache Research Center, UT Health Science Center at Houston

**History and Epidemiology**

The first clear descriptions of cluster headache came from 17th and 18th century Europe, with the first in depth account from the Dutch physician Nicolas Tulp in 1641, and the first complete account that meets all International Classification of Headache Disorders criteria from the Dutch physician Gerard van Swieten in 1745. In the early 1900s, the disease was meticulously described by the German and Swiss neurologist Paul Robert Bing and the London neurologist Willfred Harris, and modern treatments such as oxygen gas and parenteral dihydroergotamine were used by the American physician Bayard Horton. Cluster headache has enjoyed a dozen different names, from the mundane “sphenopalatine neuralgia” to the more colorful “erythroprosopalgia of Bing.” The current name of the disease was provided by the American physician E. Charles Kunkle in 1952, who noticed that the headaches tend to “cluster” together. Cluster headache was often considered a variant of migraine until very recently, and was established as its own disorder with the first International Classification of Headache Disorders (ICHD-I) in 1998. The ICHD have gone through three iterations with largely similar criteria for cluster headache throughout: only restlessness/agitation was added with the ICHD-II revision in 2004, and two new autonomic features were added in the current 2013 ICHD-III-beta revision in 20132. The current criteria for cluster headache are:

A. At least five attacks fulfilling criteria B–D
B. Severe or very severe unilateral orbital, supraorbital and/or temporal pain lasting 15–180 minutes when untreated
C. Either or both of the following:
   1. at least one of the following symptoms or signs, ipsilateral to the headache: conjunctival injection and/or lacrimation, nasal congestion and/or rhinorrhea, eyelid edema, forehead and facial sweating, forehead and facial flushing, sensation of fullness in the ear, miosis and/or ptosis
   2. a sense of restlessness or agitation
D. Attacks have a frequency between one every other day and eight per day (for more than half of the time when the disorder is active)
E. Not better accounted for by another diagnosis

Cluster headache comes in two variants, described by the ICHD-III-beta as follows:

- Episodic cluster headache: At least two cluster periods lasting from 7 days to 1 year (when untreated) and separated by pain-free remission periods of ≥1 month.
- Chronic cluster headache: Occurring without a remission period, or with remissions lasting <1 month, for at least 1 year.

Cluster headache has a prevalence of 0.1% of the population, approximately the same rate as multiple sclerosis in the United States. Cluster headache is more common in men than women at a rate of 3:1, with a typical onset between 20-40 years old. About 90% of patients have the episodic form and usually have 1-3 headaches per day, lasting between 2 weeks and 3 months, with cycles occurring once or twice per year. There is some interchange between the episodic and chronic forms, as 13% episodic cluster headache patients switch to chronic, and up to 33% of chronic cluster headaches change to episodic.

**How do I diagnose cluster headache?**

The ICHD-III-beta criteria are listed above. The pain of cluster headache is exquisite, and anecdotally is regarded by patients as more painful than migraine, kidney stones, childbirth, or multiple bone fractures. The cluster headache cycle may start and end with headaches that are milder in intensity, as if the headache cycle is ramping up and cooling down. And 30% of patients with cluster headache report a low-level of interictal discomfort between attacks.

Features that are characteristic of cluster headache are the short time to maximal pain (generally within minutes) and the circadian pattern (82% of patients have headaches at the same time every day). There are also typical headache triggers which include alcohol, nitroglycerin, heat, exercise, and naps. For episodic cluster headache, there is a characteristic circannual pattern, with cluster periods usually occurring in the spring and fall. Interestingly the headache triggers only work during the cluster period for episodic cluster headache, and have no effect in the headache-free period.

Cluster headache can be differentiated from migraine primarily based on cluster headache’s shorter duration, associated restlessness, and potential for multiple headaches per day. Many typical “migranous” and “trigeminal autonomic” symptoms are not helpful in distinguishing between migraine and cluster headache: about half of cluster headache patients have nausea, photophobia, and phonophobia (some even have auras and premonitory symptoms), and likewise about half of migraine patients have cranial autonomic symptoms.

The differential diagnosis for cluster headache includes other primary headache disorders such as migraine, paroxysmal hemicrania, and h ypnic headache; cranial neuralgias such as trigeminal neuralgia; and secondary headache disorders such as temporal arteritis, maxillary sinusitis, Tolosa-Hunt syndrome, and infections of the cavernous sinus.

**What is the pathophysiology of cluster headache?**

The cause of cluster headaches is poorly understood. About 5-10% of cluster headache patients have a family history of cluster headache, suggesting a genetic link. Presumably, cluster headache has multiple susceptibility genes. One of those genes...
may be the orexin/hypocretin receptor 2 (HCRTR2) which is implicated in sleep, narcolepsy, and hypothalamic functioning. Mutations in HCRTR2 were associated with cluster headache in two independent studies\(^9,10\), but not in a third\(^11\). Cluster headache patients are much more likely to use tobacco than the general population, and the rate of patent foramen ovale is higher, but a causative relationship with these factors has not been established.

A small proportion of cluster headaches are secondary, giving some insight into different areas of the brain that may be involved. Cluster headaches have been associated with hypothalamic and pituitary tumors, meningiomas (anywhere from the cavernous sinus to the upper cervical spine), carotid artery dissections, vascular malformations, and sleep apnea\(^12\). These associations, and the clinical features of cluster headache, suggest that there are three brain systems involved. The first is the hypothalamus, which may be the location where cluster attacks originate. Not only is the hypothalamus the site of the circadian pacemaker in the suprachiasmatic nucleus, but imaging data shows preferential activation of the posterior hypothalamus at the onset of a cluster headache\(^13\). Anatomical and functional changes of the hypothalamus have also been seen in cluster headache patients, as have alterations in hypothalamic and pituitary molecules such as orexin, melatonin, and luteinizing hormone\(^14\)\(^16\). The second system involved in cluster headache is the autonomic system, specifically the superior salivatory nucleus and the sphenopalatine ganglion, which includes molecules such as vasoactive intestinal peptide that have been shown to be altered in cluster headache. Stimulation of the sphenopalatine ganglion can trigger or abort a cluster headache attack, depending on the setting. And the third system is the trigeminal nucleus, sometimes grouped with the large cranial blood vessels and meninges (“the trigeminovascular system”), or grouped with the upper cervical dorsal horns (“the trigeminocerebral complex”). This area is likely involved in the pain component of cluster headache, and includes molecules such as calcitonin gene-related peptide, pituitary adenylate cyclase-activating peptide 38, and others that have been shown to be altered in cluster headache.

### How do I manage my cluster headache patient?

A brain MRI, with particular focus on the pituitary and cavernous sinus, is recommended in all patients according to the European Headache Federation\(^17\). Additional work-up for many cluster headache patients might include ESR and CRP for temporal arteritis, especially in the elderly. In some cases, referral to ophthalmology, otolaryngology, or dentistry can be considered. A trial of indomethacin is often warranted to rule out paroxysmal hemicrania, as the features of these two diseases are very similar, and indomethacin is completely effective in treating paroxysmal hemicrania. If indomethacin is only partially effective, you may still be dealing with cluster headache. For patients refractory to several medications, the European Headache Federation recommends vessel imaging of the head and neck (such as MRA), pituitary lab testing, and polysomnography for sleep apnea (continuous positive airway pressure has been helpful in treating headaches for some patients). For suspected secondary causes of cluster headache, please note that lesions such as pituitary microadenomas, meningiomas, and vascular malformations are common incidental findings that may be entirely unrelated to the cluster headaches. Patients should be counseled that treatment of these lesions may or may not have an effect on their headaches, and that surgical resection likely should be considered only in the most refractory cases.

Treatment options are listed in Table 1, which includes recommendations from the American Headache Society\(^18\) and the European Federation of Neurologic Societies\(^19\). As these medications have not all been tried head-to-head, a study is also included showing the percentage of patients who received “excellent” relief after trying these medications\(^20\). For abortives, oxygen gas, injectable sumatriptan, and nasal zolmitriptan are the preferred treatments. Oxygen gas should be tried at 15 L/min, via a non-rebreather mask, for 20 minutes and appears to work better if taken early in the headache attack. For bridging medications (i.e. several weeks or less), ipsilateral greater occipital nerve block with steroids plus local anesthetic can be effective for several weeks, however the exact dosage of these injected medications is not clear. For prophylactics, verapamil is generally considered first line, though it often requires high doses (240-960mg daily divided TID), so a baseline EKG, and EKG’s after each dose change and then every 6 months, are recommended.

### Cluster Headaches

<table>
<thead>
<tr>
<th>Medication</th>
<th>American Recommendation</th>
<th>European Recommendation</th>
<th>Proportion receiving “excellent” relief</th>
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<td><strong>Abortive</strong></td>
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<tr>
<td>Oxygen gas</td>
<td>A</td>
<td>A</td>
<td>56%</td>
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<tr>
<td>Sumatriptan sc</td>
<td>A</td>
<td>A</td>
<td>83%</td>
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<tr>
<td>Sumatriptan nasal</td>
<td>B</td>
<td>A</td>
<td>49%</td>
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<tr>
<td>Sumatriptan po</td>
<td>--</td>
<td>--</td>
<td>23%</td>
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<tr>
<td>Zolmitriptan nasal</td>
<td>A</td>
<td>A/B</td>
<td>51%</td>
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<tr>
<td>Zolmitriptan po</td>
<td>B</td>
<td>B</td>
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<tr>
<td>Octreotide SC</td>
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<td>Lidocaine 4-10% nasal</td>
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<td><strong>Bridge</strong></td>
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<td>Ipsilateral GONB</td>
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<td>Steroids</td>
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<td>50%</td>
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<td>Ergotamine Teratrate</td>
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<td><strong>Prophylactics</strong></td>
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<tr>
<td>Verapamil</td>
<td>C</td>
<td>A</td>
<td>48%</td>
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<td>Lithium</td>
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<td>Melatonin</td>
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<td>Baclofen</td>
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Table 1: Treatment recommendations for cluster headache based on American and European guidelines. Grade A = established as effective. Grade B = probably effective. Grade C = possibly effective. Grade U = data inadequate. GONB: Greater Occipital Nerve Block.

To look for heart block. For treatment during pregnancy and lactation, options to discuss with the patient and with obstetrics include oxygen gas and intranasal lidocaine amongst others\(^21\). Greater occipital nerve block with local anesthetic alone could also be considered; adding steroids to the injection requires more careful consideration.

For patients refractory to standard treatments, revisiting medications such as oxygen gas may also be helpful: there has been much importance placed on education of oxygen use, that it requires 15 L/min via non-rebreather for a full 20 minutes. Anecdotally, some patients require higher rates, up to 25 L/min via non-rebreather. Lifestyle changes should also be emphasized, including the avoidance of triggers such as alcohol. Other treatments not listed in the table with some data include eletriptan, frovatriptan, tizanidine, gabapentin, clonidine, botox injections, pizotifen, chlorpromazine, histamine, clomiphen, leuprolide, methylphenidate, methylsergide, dihydroergotamine (IV and nasal), and warfarin\(^8,18,22\). Alternative therapies have not shown benefit in small retrospective studies, including acupuncture, chiropracy, hypnosis, and homeopathy.
Should many medications fail to provide benefit, occipital nerve stimulation and deep brain stimulation of the posterior hypothalamus have been described\(^{23,24}\), and guidelines for their use have been proposed that include 1.2 years of refractory headaches and extensive trials of medications\(^{25,26}\). Enrollment in one of the current cluster headache trials (see below) is also an option. Patients may ask you about psilocybin and other psychedelic compounds, as some patients have found relief with sub-psychedelic dosages and a seemingly non-psychedelic formulation showed promise in a preliminary case series\(^{27}\). Additional trials of psychedelics have been proposed, but the majority of these compounds are currently listed as Schedule I drugs and thus are illegal to prescribe.

**WHAT TREATMENTS ARE IN DEVELOPMENT FOR CLUSTER HEADACHE?**

Calcitonin gene-related peptide (CGRP) is a pain signaling molecule of the trigeminovascular system that is elevated in patients with cluster headache or migraine. Antibodies for CGRP have been developed by several companies, and are now in phase 3 trials for both cluster headache and migraine. They do not appear to have the hepatotoxic effects of some of the earlier small molecule CGRP inhibitors. As of October 2016, the open clinical trial for CGRP antibodies for cluster headache, including participating trial locations and contact information, is ClinicalTrials.gov identifier: NCT02397473 (episodic cluster headache) and NCT02438826 (chronic cluster headache).

Sphenopalatine ganglion stimulation has been shown to be an effective abortive treatment for cluster headache in European studies. This stimulator is currently in trials in the United States for chronic cluster headache (ClinicalTrials.gov identifier: NCT02168764), and is arguably more attractive than other stimulators in part because it is much smaller and can be powered wirelessly through a device held at the cheek. Separately, vagal nerve stimulation has also been shown to be effective for cluster headache, and a non-invasive vagal nerve stimulator is in development\(^{28}\).
A 13 year old boy presented with altered mental status. Symptoms began the day prior to admission, with hypersomnolence and mild confusion after playing in a middle school football game. The next morning, he was forgetful, confused, and intermittently agitated. However, his family allowed him to go to school and throughout the day his symptoms worsened, progressing to lethargy. He was taken to an outside hospital, where he had serum studies, CT head, and a lumbar puncture performed. He was also given a dose of ceftriaxone. He was subsequently transferred to Dell Children’s Medical Center (DCMC) for further evaluation and management.

A couple of weeks prior to his presentation, the patient experienced upper respiratory symptoms, including rhinorrhea, nasal congestion and cough. He then developed a rash on his trunk and extremities, as well as a headache, but no fever.

A review of his medical and developmental history revealed he was a healthy boy that was not on any medications. He was a good student in the 6th grade and played school football. His social history was remarkable, as he lived in a rural setting east of Austin, with frequent exposures to several animals, including cattle, horses and bulls. He was part of a rodeo family.

On neurologic consultation, he was restless and impulsive, trying repeatedly to stand up in the hospital bed. His general exam was unremarkable except for the petechial rash which was observed more on the bilateral arms than legs, and faintly on his trunk and back. A comprehensive neurologic exam was challenging given his mental status. He was awake and alert, but oriented to person only; he was able to be redirected and follow some simple commands. His speech was fluent. There were no gross cranial nerve, motor or sensory exam abnormalities. Deep tendon reflexes were 2+ and brisk throughout and Babinski reflex was negative. There was no dysmetria. He was able to ambulate independently but at times required assistance for mild imbalance.

Review of labs and imaging obtained at the outside hospital showed normal CBC, CMP and urinalysis studies; unremarkable toxicology screens; and elevated ESR. His CSF studies demonstrated pleocytosis with normal glucose and slightly elevated protein, as well as negative gram stain. Herpes simplex virus (HSV) and West Nile virus (WNV) PCR tests were sent and pending. His CT head was interpreted as unremarkable. Post-arrest and received CPR and defibrillation, with return of spontaneous circulation after several minutes. Post-arrest and CSF WNV PCR was reported positive, and WNV antibodies for IgG and IgM were pending for confirmation.

By day 6 of hospitalization, his exam again worsened, as he developed bulbar symptoms and respiratory distress, requiring transfer to the intensive care unit and intubation. His neurologic exam was remarkable for appendicular hypertonicity and hyperreflexia. Repeat MRI brain showed radiographic worsening with restricted diffusion in the subcortical structures and bilateral frontal lobes (right > left), as well as acute hemorrhage with mass effect in the right basal ganglia and thalamic region (Figure 2).

Neurologically, he continued to deteriorate; he developed symptoms of brainstem dysfunction such as unequal pupils and poor gag. He began having autonomic changes including episodes of tachycardia and hypertension. Cardiac echo was normal. Serial CT head imaging was performed without significant progression. Continuous EEG monitoring was started to evaluate for subclinical seizures as a cause for the autonomic changes. By day 9 of hospitalization, his WNV antibodies were reported as positive for IgM, negative for IgG. He was started on interferon-alpha 2b by the infectious disease team, with hopes of improving some neurologic and respiratory function.

On day 10 of hospitalization, the patient went in to cardiac arrest and received CPR and defibrillation, with return of spontaneous circulation after several minutes. Post-arrest and thalamus (Figure 1). MRI of the cervical, thoracic and lumbar spine was unremarkable. He was started on steroid therapy as well for a presumed post-infectious or autoimmune encephalitis.

Over the next 2-3 days, his clinical presentation worsened. He became less verbal and had less frequent periods of coherence. He developed visual hallucinations. His agitation worsened, requiring treatment with Zyprexa. He had poor sleep. His coordination and balance worsened and he required assistance to walk. He did not have any seizures, though given his waxing and waning mental status, a routine EEG was performed and demonstrated generalized slowing of the background and no focal subclinical epileptiform activity. He was started on a course of intravenous immunoglobulin (IVIg) given a lack of response to steroids and deterioration of mental status. The next day, there was slight improvement in his mental status, characterized by increased alertness and ability to follow some commands. Serum and CSF WNV PCR was reported positive, and WNV antibodies for IgG and IgM were pending for confirmation.

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Imaging findings are variable and dependent on the area of neuroaxis involved with the infection. Many patients have normal neuroimaging. Interestingly, in a review by Ali et al of the brain and spinal imaging of 17 patients affected by WNV neuroinvasive disease, showed that patients with a normal MRI brain or only changes on DWI sequence had the best prognosis in terms of neurologic recovery. Those with T2 and FLAIR changes had the worst outcomes, characterized by moderate to severe neurologic deficits (5,6).

Management is largely supportive. A few therapeutic agents have been studied for use in WNV infection, including IVlg, ribavirin and interferon- alpha 2b. Of the three, treatment with interferon-alpha 2b has demonstrated efficacy in vitro and in animal models, and shown to be both protective and therapeutic. Clinical trials are ongoing; therefore it is being experimentally used, supported by its use in treatment of hepatitis C infection, a viral infection of the same Flaviviridae family. In a 2 patient report by Kalil et al, interferon-alpha 2b was started within 72 hours of presentation, and the patients both demonstrated rapid neurologic improvements within 48 hours (7,8).

Prognosis remains variable, ranging from complete recovery without residual deficits to progression to death. In a large prospective study examining neurologic outcomes in adults by Hart Jr et al, factors that influenced severity or recovery of function included age, gender and presenting manifestations (9).

REFERENCES:
1. Centers for Disease Control and Prevention- West Nile virus, CDC.gov.
With the election of Donald Trump to the presidency and his call for repeal and replacement of the ACA, many AAN members have been asking how this change, if successful, will impact the new physician payment system under MACRA.

The ACA and MACRA, Defined:

**Affordable Care Act (ACA):** Also known as “Obamacare.” Law passed in 2010. Intended to increase health insurance quality and affordability, lower the uninsured rate by expanding insurance coverage, and reduce the costs of health care.

**Medicare Access and CHIP Reauthorization Act (MACRA):** Law passed in 2015. Commonly called the “Permanent Doc Fix,” eliminates the Sustainable Growth Rate formula by establishing a new way to pay doctors who treat Medicare patients.

The first thing to know is that although both laws deal with health care, they are very different in substance and each passed Congress under very different circumstances.

In early 2010, the ACA passed with exactly zero Republican votes. Since taking over the majority in the House in 2011 and the Senate in 2015, Republicans have voted dozens of times to repeal all or part of the law. With President Trump’s campaign promises, any legislation repealing the ACA that hits his desk is sure to be enacted rather than facing the certain veto of President Obama.

MACRA is completely different. This was bipartisan legislation passed in March of 2015 on a vote of 392-37 in the House and 92-8 in the Senate. With broad support, there isn’t anyone in Congress calling for repeal of MACRA. In November of 2016, the Centers for Medicare and Medicaid Services (CMS) published the first rules on MACRA and many, including the AAN, are looking for some changes, but not a repeal.

When President Trump laid out his plans for his first 100 days in office, the repeal of some or all of the ACA was highlighted, but he still has to deal with the Senate minority. Democrats picked up two seats with victories over Republican incumbents in New Hampshire and Illinois. Senate rules require legislation to move forward with unanimous consent or reach a 60-vote majority. Republicans are likely to have just 52 votes making a total repeal of the ACA very difficult.

MACRA’s new payment system has broad congressional support and the AAN is committed to doing everything possible to ensure our members can successfully participate. MACRA is not Obamacare. Although some parts of these laws are intertwined, the impact of a repeal of the ACA will not eliminate MACRA.

Other Election Notes

- In addition to picking up two Senate seats, House Democrats will gain six seats bringing the Republican majority down to 241-194.
- At least three new House Republicans have medical backgrounds: Representatives-elect Roger Marshall is an OB/GYN from Kansas, Drew Ferguson is a dentist from Georgia, and Neal Dunn is a urologist from Florida.
- Three physicians looking for promotions from the House to the Senate failed to win on election day. Reps. Charles Boustany (R-LA), John Fleming (R-LA), and Joe Heck (R-NV) each came up short.
- Incumbent Senator Mark Kirk (R) was defeated in Illinois by Rep. Tammy Duckworth (D). Sen. Kirk, a stroke survivor, is the author of S. 1465, the Furthering Access to Stroke Telemedicine Act (FAST Act) that has been a top priority of the AAN for the last two years. We are hopeful of passing the FAST Act before the 114th Congress expires, but if it doesn’t, we will be looking for a new Senate sponsor in 2017.
- It is the first time in 100 years of senators being popularly elected that every state with a Senate seat race voted for the same party for both president and Senate.
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