



HEADACHE MANAGEMENT

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The natural history of a migraine attack

The introduction of the triptans, the revolutionary class of migraine-specific agents, was the direct result of our growing understanding of the pathophysiology of migraine; in particular, of the key role of serotonin. The triptans are highly selective agonists of the 5-HT_{1B/1D} serotonin receptors, an action that interrupts the cascade of pathophysiological processes that characterize migraine attacks.

Serotonin has long been implicated in the pathophysiology of migraine.¹ Migraineurs have an inherited impairment in the function of calcium channels that mediate the release of 5-HT (serotonin) in the central and peripheral nervous systems. Serotonin is an important neurotransmitter with vasoconstrictive actions on blood vessels. It also appears to act as a modulator that alters the level of several functions, including sensory responsiveness and motor activity.²

The pathophysiological events that lead to a migraine headache begin as early as 12 to 24 hours prior to the onset of head pain. A dysfunction in the hypothalamus, which has high concentrations of serotonin, is thought to be responsible for the prodrome, the first phase of migraine. The prodrome may be accompanied by fatigue, sleepiness, elation, food cravings, depression, irritability, and a variety of other symptoms.³ During the prodrome, patients are often aware that an attack is underway. In an electronic lock-out diary study of subjects acknowledging prodromes, Giffin noted that 83% of subjects predicted greater than 50% of attacks and if subjects reported that their prodrome “almost certainly” would predict a migraine, they were 93% accurate. Thus, in some patients, prodromal symptoms may be clinically useful.⁴

The prodrome is followed by an aura in patients who have migraine with aura (about 15% of migraineurs). Aura symptoms may include a perception of flashing lights that begin in the center of vision and expand in jagged patterns out into the peripheral vision. Symptoms may be somatosensory, such as numbness and tingling in the lips or fingers; they may also involve a profound alteration of the perception of space and time.

The aura is caused by an electrical depolarization called cortical spreading depression (CSD), a phenomenon first described in animal studies by *Leao* in 1944.⁵ During CSD, a depression in neuronal activity is followed by a reduction in blood flow, usually beginning in the occipital region, which moves across the cerebral cortex at a rate of 2-3 mm per minute.⁶ A study

by *Hadjikhani et al* employed high-field functional magnetic resonance imaging (MRI) to demonstrate this phenomenon in three human subjects who had migraine with aura.⁷ They observed blood oxygenation-level-dependent changes that were coincident with the onset of the aura. The investigators concluded that their results strongly suggest that the electrophysiological events of CSD generate the aura in human visual cortex.

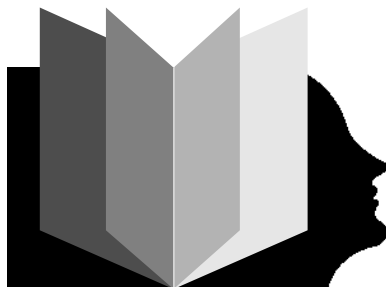
There is a considerable debate on the relationship between the aura and the initiation of the pain phase of migraine. *Bolay et al* discovered a neural mechanism in migraine that couples extracerebral blood flow to brain events.⁸ They showed that CSD activates trigeminovascular afferents that lead to cortical meningeal and brainstem events consistent with the development of headache. *Moskowitz et al* demonstrated that CSD results in the release of neuropeptides, such as substance P, CGRP, and neurokinin A, that produce sterile neurogenic inflammation;⁹ this sensitizes first-order neurons to respond to previously innocuous stimuli.¹⁰ Impulses coming from sensitized peripheral nociceptors then activate second-order neurons and initiate their sensitization; this process may mediate the development of ipsilateral cutaneous allodynia. The sensitized second-order neurons then activate and sensitize third-order neurons, which subsequently mediate cutaneous allodynia on the contralateral head and ipsilateral forearm. Patients with cutaneous allodynia experience an extreme sensitivity to touch. They may complain that they can't wear a watch or jewelry, or that their “hair hurts.” *Burstein et al* observed that this peripheral sensitization may provoke subsequent intracranial hypersensitivity that contributes to the headache phase, although the relationship is not fully understood.¹¹

Intracranial sensitization appears to be related to activation of an area of the brainstem. Using positron emission tomography (PET), *Weiller et al* discovered a “migraine generator” in the dorsal raphe of the brainstem.¹² Activation of this brainstem region is specific to migraine and is not present in cluster headache or other types of head pain. Significantly, the brainstem activation observed by *Weiller et al* persisted after the administration of sumatriptan relieved the headache, photophobia, phonophobia, and other autonomic symptoms.¹² This phenomenon suggests a mechanism for migraine recurrence (see the article on migraine recurrence in this issue).

The headache phase may last from four to 72 hours; headache duration may be related to continued brainstem activation. The headache of migraine begins as a mild headache that escalates over time into a moderate to severe headache with associated symptoms diagnostic of

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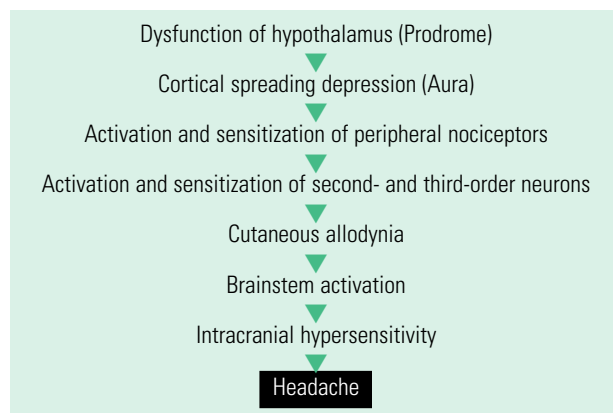
IHS migraine. Numerous studies have demonstrated that abortive treatment initiated during this mild pain phase is more likely to achieve a pain-free state than if the same treatment were initiated when the headache is moderate to severe.¹³⁻¹⁵ The “early intervention” strategy is more effective probably because it aborts the headache before significant central sensitization has occurred.

Once the pain has run its course, there is a postdrome, where the pain is resolved but other unpleasant symptoms may linger. Patients often describe a feeling of being “hung over.” Sensory perception and cognition may remain impaired and GI symptoms (nausea, queasiness, and anorexia) and sore muscles may persist for a day or two. Postdrome symptoms may require treatment in some patients in order to shorten the duration of headache-related disability.

Figure 1.

The pathophysiologic course of a migraine attack

1



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Chronic daily headache: an overview

Chronic daily headache (CDH) affects 4% to 5% of the population and encompasses a spectrum of primary headache disorders that occur on a daily or near-daily basis.¹ CDH is frequently encountered in clinical practice, in part because CDH patients are more likely to seek medical care than other patients with headache. In a series of 693 new patients consecutively presenting to a specialized headache clinic, 247 (36%) had CDH of at least two months' duration.² We present here a brief overview of CDH, with a description of the long-duration (> 4 hours) primary CDH types.

In the second edition of *The International Classification of Headache Disorders*, the International Headache Society (IHS) does not fully address the very frequent primary headache disorders, although it does define in detail two of the most common of these headaches: transformed migraine and medication-overuse headache.³ CDH includes a variety of diagnoses and there have been several attempts at classification. There is a general agreement that CDH refers to headaches that occur \geq 15 days per month. *Silberstein et al* classify the various subtypes of CDH into primary and secondary categories (Table 1). They further categorize primary CDH by average duration (greater or less than 4 hours).⁴ There is evidence that each primary subtype is a distinct biologic entity with a unique pathogenesis.^{1,5} Others have proposed similar classifications.⁵

Table 1.

Classification of CDH

(adapted from Silberstein et al)⁴

Primary CDH (frequency: \geq 15 days/month; average duration: > 4 hours)

- Transformed migraine
- Chronic tension-type headache (CTTH)
- New daily persistent headache (NDPH)
- Hemicrania continua

Primary CDH (average duration < 4 hours)

- Cluster headache
- Chronic paroxysmal hemicrania
- Hypnic headache
- Idiopathic stabbing headache

Secondary CDH

- Post-traumatic headache
- Cervical spine disorders
- Headache associated with vascular disorders: arteriovenous malformation; arteritis, including giant cell arteritis; dissection; subdural hematoma
- Headache associated with nonvascular intracranial disorders: intracranial hypertension, infection (Epstein-Barr virus, HIV), neoplasm
- Other: temporomandibular joint disorder; sinus infection

Transformed migraine (TM)

Transformed migraine, one of the most common types of CDH, was first described by Mathew in 1982.⁶ It is defined as daily or near-daily headache in a patient with a history of episodic migraine. Patients typically present with headaches that are increasing in frequency and that may or may not include migrainous features.⁵ CDH may have developed when interictal headaches became increasingly frequent between attacks of migraine.⁷ The reason for the spontaneous transformation of episodic migraine into chronic migraine is unknown. A study by *de Tommaso et al* suggests that patients with transformed migraine have an abnormal cortical processing of nociceptive input, which leads to a chronic state of pain.⁸ Table 2 lists diagnostic criteria for TM proposed by *Silberstein et al* in 1994.

Table 2.

TM diagnostic criteria (adapted from Silberstein et al)⁹

- A. History of episodic migraine meeting IHS criteria
- B. Daily or almost daily headache (>15 days per month) for > 1 month
- C. Average headache duration of 4 hours/day (if untreated)
- D. History of increasing headache frequency with decreasing severity of migrainous features
- E. Secondary disorders as headache causes are ruled out

Although transformed migraine is widely recognized as a clinical entity, opinions differ on how to classify TM. *Mathew et al*,¹⁰ *Silberstein et al*,⁴ and *Mendizabal and Rothrock*⁵ regard primary transformed migraine and medication-overuse headache as subpopulations of transformed migraine, while the IHS classification tends to regard them as distinct entities.³ Certainly, the distinction between the two is clinically important, because the patient with medication-overuse headaches is unlikely to respond to preventive medications until excessive medication use has ceased. The IHS classification prefers the term chronic migraine to transformed migraine, regarding it as a complication of episodic migraine. They note however, that their criteria "require further study."³

Mathew et al first noted that approximately 80% of TM patients overuse acute headache medications.¹⁰ Roughly the same percentage of TM patients also have clinical depression, which often improves when medication overuse stops and the headaches ameliorate.⁴ Migraineurs who self-treat are often unaware of how many different medications they take; the medications may fill a shopping bag. The phenomenon of medication-overuse headache occurs when the daily or near-daily use of analgesics renders the mechanism of migraine dependent on a continuous supply of analgesics. Eventually, falling analgesic blood levels trigger the headache mechanism, producing a rebound headache which leads to the ingestion of still more analgesics. Rebound headaches have been associated with virtually all analgesics

including ergotamine, opioids, triptans, aspirin and other NSAIDs, acetaminophen and combination analgesics. If a patient takes prescription or OTC analgesics three or more days per week, the possibility of medication-overuse headache should be considered.

Chronic tension-type headache (CTTH)

Episodic tension-type headache (ETTH) may also develop into chronic tension-type headache. They are usually bilateral, mild or moderate in severity, and not aggravated by mild physical activity, such as walking up stairs.⁹ To meet the diagnostic criteria for CTTH, a patient must have a prior diagnosis of ETTH, experience headaches ≥ 15 days per month on average over the past six months, with an average headache duration of > 4 hours per day (if untreated). Although patients with CTTH may also experience occasional migrainous symptoms, such as nausea, photophobia, or phonophobia, the IHS Classification Committee considers CTTH to be a distinct clinical entity. This is supported in a study by Rothrock *et al*, who observed that patients with episodic migraine or transformed migraine responded to divalproex sodium, while patients with CTTH did not.¹¹ Others have debated this assertion, noting that CTTH has migrainous features, may be triggered by the same factors that trigger migraine, and may also be associated with medication overuse.¹²

New daily persistent headache (NDPH)

NDPH is the sudden development (over less than three days) of an unremitting headache in patients without a history of tension-type headache, migraine, or head trauma. Patients often remember the exact day of onset. The character of the head pain shares features of tension-type headache and migraine without aura.⁵ Despite its resemblance to CTTH, it is not clear whether NDPH is related to the former disorder. There is some evidence that NDPH is a post-viral syndrome, but this is by no means universally accepted.¹³ Because of its ambiguous features, Silberstein *et al* suggest that NDPH is actually a heterogeneous disorder.⁴

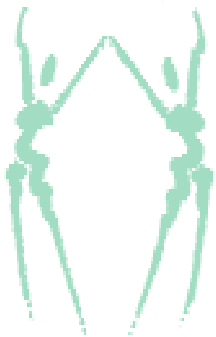
Hemicrania continua (HC)

This rare CDH syndrome was first described by Sjaastad and Spierings in 1984.¹⁴ Hemicrania continua is characterized by a unilateral, continuous, moderately severe headache that varies in

intensity and may rarely alternate sides. The pain of HC occurs most frequently over the temporal and frontal areas; it may be accompanied by stabbing headaches. When pain worsens, it is often accompanied by autonomic symptoms, such as ptosis, nasal congestion or rhinorrhea, eyelid edema, tearing, conjunctival injection, or sweating. Episodic hemicrania continua may be mistaken for cluster headache, but the former has more frequent attacks of briefer duration.¹⁵ There appears to be three forms of this disorder: a remitting form with headache phases lasting weeks to months separated by prolonged pain-free periods, an unremitting form that evolves from the remitting form, and a form that is unremitting from onset.^{15,16} Although exceptions have been described, HC almost invariably responds to treatment with indomethacin.

Treatment of patients with CDH may be difficult, because the vast majority of patients overuse headache medications and/or have comorbid depression. In the next issue of *Challenges in Headache Management*, we will review treatment strategies for the various manifestations of chronic daily headache.

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Approximately 80% of transformed migraine patients overuse acute headache medications. 🍀 🍀 🍀 🍀

Migraine recurrence with the triptans: key issues and answers

The evaluation of efficacy in the acute treatment of migraine includes not only initial improvement, but the absence of headache recurrence after initial improvement. Surveys have shown that patients place a high value on low recurrence, rating it more important than good tolerability (Table 1).^{1,2} Conversely, headache recurrence is frequently cited as a principal reason for patient dissatisfaction with treatment.³

How should headache recurrence be defined? Should recurrence be limited to patients who initially become headache free or should it include headaches that worsen from mild to moderate or severe within a given time period? Is a migraine that returns at 48 hours a recurrence or a new headache? Are worsening and recurrence different physiological phenomena? There are no definitive answers to these questions, although Goadsby argues that, from a clinical point of view, it is reasonable to consider recurrence as a headache that initially improves and then worsens within a 24-hour period.⁴

Table 1.

Features of migraine medication ranked by importance¹

1

Feature	Mean rating*
■ Provides quick headache relief	9.91
■ Decreases head pain	9.87
■ Decreases likelihood of recurrence	9.81
■ Does not cause nausea	9.14
■ Decreases nausea	8.75
■ Decreases vomiting	8.37
■ Decreases sensitivity to light	8.28
■ Orally administered	7.97
■ Decreases visual problems	7.77
■ Does not cause drowsiness	7.66

*Based on a 10-point scale
(1 = not at all important; 10 = extremely important)

Headache recurrence is a problem common to all acute migraine medications, including the triptans and NSAIDs.⁵ Among current therapies, dihydroergotamine appears to have the lowest recurrence rates.⁴ The headache recurrence rates among the triptans differ widely and there have been several attempts to measure these rates.^{4,5} Methodological problems render the results somewhat suspect, but certain trends have emerged. (One of the problems with a few studies is that recurrence rates were reported

as a percentage of the total number of patients treated, including nonresponders.) Table 2 shows a comparison of pain-free response rates and recurrence rates compiled from a variety of triptan trials. A similar comparison was conducted by Gawel and Tepper; they found a clear association between a drug's half-life and the rate of headache recurrence. Sumatriptan and rizatriptan, which have half-lives of approximately 2 hours, had recurrence rates of approximately 34%. By comparison, frovatriptan, which has a half-life of approximately 26 hours, had a recurrence rate of 9-14% in this series.⁶ Naratriptan, which has a half-life of approximately 6 hours, was also shown to have a lower recurrence rate than sumatriptan in a double-blind crossover study of patients with frequent recurrence of their headaches.⁷ Another direct, comparative study showed naratriptan to have a lower recurrence rate than rizatriptan.⁸ However, debate exists regarding recurrence rates of the triptans being solely dependent on drug half-life, since longer half-life triptans generally have lower pain-free rates at two hours, and consequently have smaller populations in which pain can recur.

Triptan half-lives appear to affect recurrence rates, but is this the whole story? *Geraud et al* studied the relationship of the clinical, pharmacological, and pharmacokinetic properties of the triptans to headache recurrence.³ They evaluated activity at the 5-HT_{1B} and 5-HT_{1D} receptors, elimination half-lives, and clinical efficacy of each triptan. Clinical data were derived from 31 placebo-controlled major efficacy studies. Mean headache response and therapeutic gain were calculated at the time points used to define recurrence in each study. Data for binding affinity and potency were derived from an *in vitro* pharmacologic study, while half-lives were derived from each product's package insert. Rank correlation with recurrence rate was calculated for each test parameter. Results showed that elimination half-life and headache recurrence were inversely correlated ($r = -1.0$; $p = .0016$). There was also a significant inverse correlation between potency at the 5-HT_{1B} receptor ($r = -0.68$; $p = .034$), but not at the 5-HT_{1D} receptor ($r = -0.20$; $p = .54$). Binding affinities for the 5-HT_{1B} and 5-HT_{1D} receptors were not correlated with recurrence, nor was initial clinical response. The investigators concluded that the triptans with long half-lives and greater potency at the 5-HT_{1B} receptor had the lowest rates of headache recurrence. Goadsby suggests that lipophilicity, which was not studied by *Geraud et al*, might also be associated with a low recurrence rate.⁴ He noted that eletriptan, the most lipophilic of the triptans, has a low rate of recurrence.

Can the relatively high recurrence rates associated with the triptans be reduced? *Ferrari et al* found that administering a second tablet of sumatriptan at 2 hours after an attack did not increase initial efficacy and neither prevented nor delayed migraine recurrence.⁹ However, in two studies *Krymchantowski et al* found that the concomitant administration of an NSAID with sumatriptan significantly reduced the headache recurrence rate.^{10,11} In the first study, the subjects were 50 migraineurs who had treated at least 10 attacks with 100 mg PO sumatriptan, which was effective in at least eight attacks.¹⁰ The subjects also experienced recurrence within 24 hours in at least five of the treated attacks. They were then treated with sumatriptan 100 mg plus tolfenamic acid 200 mg PO during the first 60 minutes of an attack. A total of 240 migraine attacks were treated, with a recurrence rate of 23.8%, compared with a baseline recurrence rate of 62.5% on sumatriptan alone.

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Table 2.

Drug	mg	N	Pain-free at 2 hrs: %(CI)	Recurrence: %(CI)
Sumatriptan	25.0	361	21 (17-25)	34 (27-41)
	50.0	367	28 (23-32)	34 (27-40)
	100.0	962	27 (24-30)	34 (25-42)
Zolmitriptan	2.5	438	25 (21-29)	31 (26-37)
	5.0	936	32 (29-35)	28 (24-32)
Naratriptan	2.5	799	23 (20-26)	25 (22-29)
Rizatriptan	5.0	1682	30 (28-32)	39 (36-42)
	10.0	2485	40 (38-42)	37 (34-39)
Eletriptan	40.0	1870	27 (25-29)	21 (19-24)
	80.0	1393	33 (31-35)	20 (17-23)
Almotriptan	12.5	719	36 (32-39)	26 (22-30)
Frovatriptan	2.5	1862	NA	20 (18-23)

(adapted from Ferrari et al)⁵

2

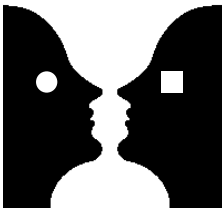
*NA = Not available

The second study included 67 subjects who had treated eight migraine attacks successfully with 100 mg sumatriptan, but had experienced recurrence in at least five attacks (62.5%).¹¹ The subjects received sumatriptan 100 mg and naproxen sodium 550 mg to treat four consecutive moderate or severe migraine attacks. With the combination therapy, the recurrence rate decreased to 14.2% (38 out of 268 attacks; p<0.0001). The investigators then studied two randomly selected groups of 13 patients each from the 67 subjects evaluated initially. They were given sumatriptan 100 mg plus naproxen sodium 550 mg or placebo in a double-blind design to treat three consecutive migraine attacks. Each group treated 39 attacks. The recurrence rate among subjects taking sumatriptan plus placebo was 59% (23 out of 39 attacks), while the recurrence rate in the group taking sumatriptan plus naproxen was 25.5% (10 out of 39 attacks; p<0.0003). The investigators concluded that sumatriptan plus naproxen sodium significantly decreases migraine recurrence compared with sumatriptan alone.

While the triptans have certainly revolutionized the treatment of migraine, the problem of headache recurrence remains. It is common to all acute treatments; it may occur in up to one-third of attacks, and is perceived by patients as a treatment failure.⁴ The recurrence rate differs from drug to drug and from patient to patient, yet studies suggest that the rate can be reduced. In particular, achieving pain-free efficacy through early intervention during the mild pain phase has been associated with lower recurrence rates. Additionally, the administration of a triptan with a long half-life may suffice in some patients; in others, the concurrent administration of an NSAID or switching to DHE may be helpful.

Headache recurrence is a problem common to all acute migraine medications, including the triptans and NSAIDs.

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N onpharmacologic approaches to migraine prevention

For many migraine patients, a multimodal therapeutic approach to their headaches includes one or more nonpharmacologic preventive therapies that may or may not have been recommended by their physicians. Alternative therapies have received a great deal of attention in recent years, in part because of improved patient-to-patient communication facilitated by the internet and in part because of a general trend encouraging patients to “take control of their own headaches.”*

Some nondrug approaches are eminently sensible, such as avoiding migraine triggers. Others are viewed by physicians with understandable skepticism. A few have been evaluated in controlled trials and found to be effective. Table 1 gives some idea of how disparate these therapies can be, from the controversial (clinical ecology¹) to the increasingly accepted (magnesium and feverfew). The placebo effect undoubtedly plays a role in the apparent success of some of these therapies, but this is also true of conventional drug therapies for migraine. Patient support groups generally take a hands-off approach: “If they work for you, that’s great.” At the same time they warn patients to be suspicious of practitioners offering very expensive forms of nonmedical therapy.¹

Table 1.
Types of nondrug migraine therapies¹

1

Relaxation methods

- Biofeedback training
- Progressive muscle relaxation
- Hypnosis and self-hypnosis
- Yoga
- Autogenic training
- Creative visualization

Nutritional regimens

Exercise

Psychotherapy

Physiological methods

- Oxygen therapy
- Carbon dioxide therapy
- Massage therapy
- Acupuncture/acupressure
- TENS (transcutaneous electrical nerve stimulation)
- Hot or cold compresses
- Osteopathy or chiropractic
- Clinical ecology
- Feverfew
- Fish oil
- Magnesium

Migraine is characterized by a heterogeneity of symptoms, so it isn’t surprising that patients seem to benefit from such a diversity of treatment approaches. Among the nondrug approaches that have been subjected to rigorous testing are magnesium and feverfew; both have shown somewhat promising preliminary results. *Trautinger et al* found that after oral loading, magnesium retention occurs in patients with migraine but not in controls, suggesting that patients with migraine have a systemic magnesium deficiency.² Subsequent studies evaluated magnesium in both the acute treatment and prophylaxis of migraine. In a double-blind, placebo-controlled parallel-group trial, *Wang et al* studied oral magnesium oxide prophylaxis in children and adolescents with frequent migrainous headaches.³ The subjects were randomly assigned to receive either magnesium oxide (9 mg/kg/day PO three times daily with food) (n=58) or matching placebo (n=60) for 16 weeks. The primary outcome criterion was the number of headache days during each of eight two-week intervals. Of those enrolled, 86 (42 magnesium and 44 placebo) completed the analysis. In an intent-to-treat analysis, there was a statistically significant decrease over time in headache frequency in the magnesium group (p=0.0037), but not in the placebo group (p=0.086), although the slopes of these two lines were not significantly different from each other. The magnesium group also had a significantly lower headache severity (p=0.0029). The authors conclude that, while the results were not unequivocal, they were promising enough to warrant further investigation.

Begal et al studied intravenous magnesium sulphate in the acute treatment of migraine with and without aura in a randomized, double-blind, placebo-controlled study.⁴ Patients were randomly assigned to receive either magnesium sulphate 1000 mg intravenously or 10 mL of 0.9% physiological saline. The investigators used seven parameters of analgesic evaluation and an analogue scale to assess nausea, photophobia, and phonophobia. In the migraine without aura group, there was no statistically significant difference in pain relief or in relief of nausea, but there was a significantly lower intensity of photophobia and phonophobia. In the migraine with aura group, patients receiving magnesium had a statistically significant improvement in pain and all associated symptoms compared with controls; the analgesic therapeutic gain was 36.7% at 1 hour. The authors conclude that magnesium sulphate can be used for the treatment of all symptoms in migraine with aura or as an adjuvant therapy for associated symptoms in migraine without aura.

Feverfew (*Tenacetum parthenium* L.), an herb related to the chrysanthemum, is one of the more extensively documented natural treatments for migraine. The herb is available as an extract in tablets or capsules to be taken daily. The recommended dose is 100 mg/day. *Ernst and Pittler* conducted a meta-analysis of randomized, placebo-controlled, double-blind trials of feverfew preparations for the prevention of migraine.⁵ In addition to efficacy, they evaluated safety and the methodological quality of the trials. They found six trials that met their inclusion criteria; their results favored feverfew over placebo. They also found only mild and transient adverse effects with feverfew and few other safety concerns. The authors concluded that feverfew is likely to be effective in migraine prevention.

HEADACHE MANAGEMENT

CHALLENGES IN HEADACHE MANAGEMENT

Nonpharmacologic
approaches to
migraine prevention

Continued from page 7

Physicians who treat migraine should not necessarily view unconventional nondrug therapies as an assault on good medical practice. 🍀 🍀 🍀 🍀 🍀

Physicians who treat migraine should not necessarily view unconventional nondrug therapies as an assault on good medical practice. Most patients who use nondrug therapies don't do so because they are dissatisfied with their medical care. Typically, they view alternative therapies as complementary to, but not replacements for, their usual migraine medications. Physicians should certainly be aware of any unconventional therapies their patients may be using, so they can be evaluated for safety and compatibility with their migraine medications and treatment plans.

* This trend is reflected in the titles of self-help books directed at migraine patients, such as *Taking control of your headaches: how to get the help you need*. (New York: The Guilford Press, 1995). The book is described on its cover as "A clinically tested approach that puts you in charge."

† Clinical ecologists are medical professionals who treat "environmental illness," which is defined as the body's response to a wide variety of allergens and toxins. Clinical ecology is controversial because our current understanding of migraine is that the condition is a primary disorder of brain chemistry and is not an environmental illness.

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