

# Diagnosing and Managing Migraine

An evidence-based review of the assessment and treatment of this prevalent, disabling condition.

**ABSTRACT:** Roughly 90% of the U.S. population will develop a headache within their lifetime, and headache disorders account for more disability-adjusted life-years than all other neurologic disorders combined. Among primary headache disorders, the two most common are tension-type headache and migraine, with migraine identified as the most disabling. Here, the authors describe the importance of differentiating primary and secondary headache disorders and discuss the pathophysiology; clinical assessment; and outpatient management of the debilitating migraine headache, summarizing both acute and prophylactic treatment strategies that can substantially reduce associated disability.

**Keywords:** headache, migraine, neurologic disorder, primary headache, secondary headache, tension-type headache

It's estimated that 90% of the U.S. population will develop a headache within their lifetime.<sup>1</sup> An analysis of the Global Burden of Disease Study 2015 found that headache disorders accounted for more disability-adjusted life-years worldwide than all other neurologic disorders combined.<sup>2</sup> Since patients with migraines often appear healthy, they are frequently subject to discrimination and stigmatization. People have trouble understanding the debilitating nature of migraines, which can negatively affect every aspect of life.<sup>3</sup> The first step in evaluating patients with a headache disorder is to determine whether the disorder is primary or secondary in order to ensure the patients receive appropriate and timely treatment.

This article provides an overview of migraine pathophysiology, incidence, prevalence, distribution, diagnosis, and management in the outpatient primary care setting. It also focuses on the essential role of nurses in helping patients achieve long-term control over this debilitating condition. Nurses are often the patient's first and most frequent clinical contact. Nursing assessment and ongoing management are thus critical for optimal patient outcomes.

## PRIMARY VS. SECONDARY HEADACHE DISORDERS

**Primary headache disorders** are those in which the headache and its associated features constitute the disorder itself. These include tension-type headache, which is the most common, affecting 38% of the population; migraine, which is the most debilitating, affecting 12% of the population; and trigeminal autonomic cephalalgias, which include cluster headaches and others.<sup>1</sup> (See Table 1.)<sup>4</sup> Primary headache disorders are often misdiagnosed and, as a result, treatment plans fail to provide relief. Although the lifetime consultation rate for migraine is relatively high, many patients report never receiving a diagnosis of migraine from a health care professional.<sup>5</sup> The third edition of the International Classification of Headache Disorders (ICHD-3) lists over 14 primary headache disorders in addition to migraine, tension-type headache, and cluster headache.<sup>4</sup> Patients whose primary headache disorder remains refractory to treatment may benefit from a referral to a headache specialist. The United Council for Neurologic Subspecialties certifies physicians in the United States and Canada with expertise in the treatment of headache disorders. Nonetheless,

there is a conspicuous shortage of headache medicine specialists in both countries, with marked geographic discrepancies.

**Secondary headaches**, unlike primary headaches, are symptomatic of an exogenous etiology and often require urgent or emergent attention (see *Secondary Headaches: Early Recognition and Intervention*<sup>6</sup>). These include headaches resulting from the following conditions<sup>4</sup>:

- head trauma or injury
- cranial or cervical vascular disorders, such as ischemic events, intracranial hemorrhage, vascular malformation, arteritis, dissection, or thrombosis
- nonvascular intracranial disorders, such as high or low cerebrospinal fluid pressure, neoplasm, or seizure
- substance use or withdrawal, such as medication overuse headache
- infection
- disorders of homeostasis, such as hypoxia or hypertension
- disorders of the cranium, neck, eyes, ears, nose, sinuses, teeth, mouth, or other facial or cervical structures
- psychiatric disorders

### THE HIGH COST OF MIGRAINES

While primary headache disorders may not require urgent care, these disorders, particularly migraine, impose a substantial burden in terms of direct and indirect costs, including not only health care resources but also lost productivity, which is not surprising given that migraines tend to affect otherwise healthy young and middle-aged people.<sup>7</sup> The Migraine Research Foundation estimates that annual U.S. health care and lost productivity costs associated with migraine are as high as \$36 billion.<sup>8</sup>

**Severe impairment.** A 2007 American Migraine Prevalence and Prevention (AMPP) study reported results of a validated, self-administered headache questionnaire mailed to a stratified random sample of 120,000 U.S. households.<sup>9</sup> Nearly 65% of households responded, representing a total of 162,576 household members ages 12 or older, 18,968 of whom met the ICHD-2 criteria for migraine. The majority (62.7%) of respondents who experienced migraine reported having one to four headache days per month, 53.7% reported experiencing severe impairment or requiring bed rest, and more than 35% indicated that, over a three-month period, they'd had to restrict activity for at least one day due to headache.<sup>9</sup>

**Anxiety and depression** commonly coexist with migraines.<sup>10</sup> Patients may worry about when the



Original art by Karen Lee-Roig, who has migraine. Lee-Roig says about her artwork, "In this piece, the darkness associated with the 'migraine eye' overshadows the light, representing symptomatic days dominating the daily life of the migraine sufferer."

next migraine will occur and how it will interrupt their day.

**Lost work and productivity.** A follow-up study published in 2008 and based on the 2007 AMPP data focused on self-reported lost productive time—that is, the sum of missed hours plus reduced productivity hour equivalents, or "presenteeism" revealed in the data, which captured both hours per week absent from work and reduced productivity hour equivalents due to migraine.<sup>11</sup> The results of this study indicated that respondents with migraine lost substantial amounts of work time: of those who worked for pay, 38% had lost time due to headache in the preceding two weeks—on average, 4.7 hours per week—with "presenteeism" accounting for roughly 75% of headache-related lost productive time.<sup>11</sup>

**Burden on family, finances, career, and overall health.** The Chronic Migraine Epidemiology and Outcomes Study, a prospective, longitudinal web-based survey conducted between September 2012 and November 2013, was designed to characterize the impact of migraine on a U.S. sample of people with migraine.<sup>12</sup> The 19,891 respondents who met the ICHD-3 criteria for migraine were invited to complete the family burden module of the survey, designed to assess the impact of migraine on participation in or enjoyment of family activities; spouse or partner interactions; parent-child interactions;

**Table 1.** Comparison of Primary Headache Disorders<sup>4</sup>

Headache	Duration	Location	Severity	Associated Symptoms
Tension type	30 minutes to 7 days	Bilateral	Mild or moderate; pressing or tightening (nonpulsating) quality	Not aggravated by activity; no nausea or emesis; either photophobia or phonophobia
Migraine	4 to 72 hours in adults; 2 to 72 hours in children	Unilateral	Moderate or severe; pulsating quality	Aggravated by activity; nausea, emesis, or both; photophobia and phonophobia
Cluster (trigeminal autonomic cephalalgia)	15 minutes to 3 hours; from 1 episode every other day to 8 headaches per day	Unilateral	Severe or very severe	Sense of restlessness or agitation; at least one of the following, ipsilateral to the headache: <ul style="list-style-type: none"> <li>• conjunctival injection and/or lacrimation</li> <li>• nasal congestion and/or rhinorrhea</li> <li>• eyelid edema</li> <li>• forehead and facial sweating</li> <li>• miosis, ptosis, or both</li> </ul>

finances; and overall health of the person experiencing the migraine, as well as the spouse or partner, and any children.<sup>12</sup> A total of 13,064 respondents who experienced either episodic (11,944) or chronic (1,120) migraine provided family burden data.<sup>12</sup> Findings indicated that respondents believed migraines negatively affected numerous aspects of their lives, with 15% to 20% reporting detrimental effects on relationships—domestic, romantic, and parental—as well as on finance, education, and career. About half felt they would be better parents if it were not for the migraines. One-third indicated that migraines had negatively affected their career and worried about their long-term financial security on account of migraines. More than 3% indicated that migraines had influenced their decision not to have children, to delay having children, or to have fewer children.

### MIGRAINE PATHOPHYSIOLOGY

Migraine is associated with multiple genes in conjunction with epigenetic triggers. Epidemiological studies show a pronounced familial link, though single gene mutations have been identified only for rare familial hemiplegic migraine syndromes.<sup>13</sup>

While the pathophysiology of migraine is not completely understood, decades of clinical research have shown that it is not a simple vascular phenomenon, but rather a multifactorial neurovascular disorder that varies widely in presentation, incorporating structures throughout the cranium as well as nerves and blood vessels outside the skull. Neuroimaging and electrophysiological studies demonstrate involvement of the hypothalamus, thalamus, cortex, trigeminal nerves, and upper cervical nerves over the various phases of a migraine.<sup>14-17</sup> The hypo-

thalamus regulates hunger and satiety, thirst, sleep-wake cycles, body temperature, and emotions, and releases hormones that control the pituitary gland. The thalamus relays all sensory information except for olfaction to the cortex, transmitting pain, visual, and auditory information. Within the brainstem, the nuclei of cranial nerves III to XII, as well as the trigeminal nucleus caudalis, and other nuclei process pain and autonomic functions, such as vomiting.

**Migraine prodrome.** Patients may experience a prodromal phase up to 48 hours before other migraine symptoms develop.<sup>4</sup> Prodromal features commonly include fatigue, difficulty concentrating, neck pain, photophobia, phonophobia, blurred vision, yawning, and pallor.<sup>4</sup>

**Migraine aura.** A brief visual, sensory, or other neurological symptom that precedes or accompanies migraine in some patients, the migraine aura is postulated to be the result of a phenomenon known as cortical spreading depression (CSD).<sup>18</sup> A slow wave of electrical excitation followed by depression of neuronal firing originates in the occipital lobe and travels anteriorly across the cerebral cortex. Along with electrical signaling, a wave of vasodilation and increased cerebral blood flow (hyperemia) lasts a few minutes followed by vasoconstriction (oligemia) lasting one to two hours. First described in experimental animals, these changes have been demonstrated in humans via functional neuroimaging techniques.<sup>19</sup> CSD in the occipital lobe accounts for visual aura, and the anterior propagation of CSD explains other aura symptoms.<sup>20</sup>

When present, the migraine aura typically includes one or more of the following features<sup>4</sup>:

- visual changes, such as sparkling or flashing lights, zigzag lines, homonymous hemianopia,

tunnel vision, or distortion (monocular vision changes, such as scotoma, characterize retinal migraines)

- speech or language difficulty
- sensory disturbances, such as paresthesia or numbness, arising from the cerebral cortex
- dysarthria, vertigo, tinnitus or other hearing changes, diplopia, ataxia, or decreased level of consciousness (all manifestations of a brainstem aura)
- motor weakness, which characterizes a hemiplegic migraine

Each aura symptom gradually evolves over five to 60 minutes.<sup>4</sup>

The migraine aura can occur either with or without headache.<sup>21</sup> A 1996 nosographic analysis of migraine aura in a general population sample of 4,000 found that of the 163 subjects who experienced migraine with aura, 62 (38%) experienced aura with and without headache, whereas seven (4%) experienced typical aura without headache, a phenomenon previously known as acephalgic migraine, migraine equivalent, or migraine accompaniment.<sup>21</sup> In the absence of headache pain, these

neurologic symptoms have a large differential diagnosis and are often challenging to diagnose. Fortunately, once diagnosed, they usually respond well to typical migraine treatment.

**Migraine episode.** As the migraine episode progresses, nerves innervating the meninges and cerebral arteries converge with sensory input from the neck and scalp in the trigeminocervical complex, ascending in the brainstem to the thalamus and the cerebral cortex and eliciting the perception of pain and associated migraine symptoms. Hyperexcitability and dysfunctional pain processing throughout these pathways perpetuate the pain process through central sensitization,<sup>22</sup> which is heightened reactivity of the nervous system that continues to generate pain in the absence of peripheral input,<sup>23</sup> potentially producing chronic pain. Numerous neurotransmitters and neuropeptides are involved in this complex process, including norepinephrine, glutamate, and calcitonin gene-related peptide (CGRP),<sup>23</sup> in addition to serotonin,<sup>24</sup> dopamine,<sup>25</sup> and possibly  $\gamma$ -aminobutyric acid (GABA).<sup>26</sup>

The headache phase of migraine lasts up to 72 hours,<sup>4</sup> though the mechanism by which it resolves

## Secondary Headaches: Early Recognition and Intervention

The SNNOOP10 mnemonic can provide guidance.

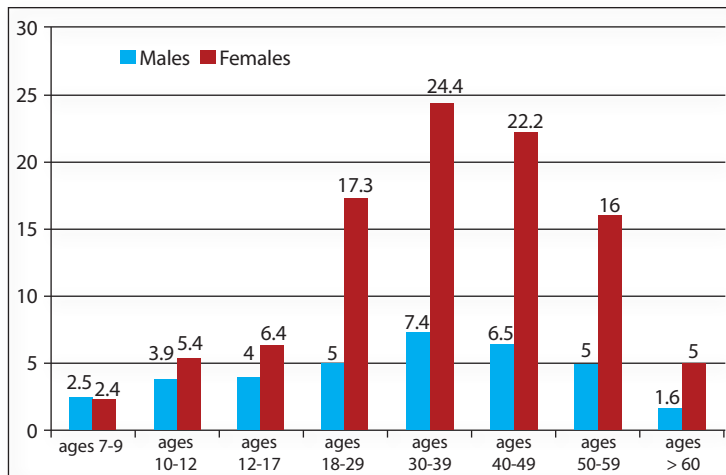
Early recognition and intervention in secondary headaches can be lifesaving. These headache types are relatively uncommon, as only an estimated 18% of people worldwide who experience a headache have a secondary headache disorder.<sup>6</sup> The likelihood of encountering a patient with a secondary headache is greater in the emergency setting than in primary care. A good history and physical examination are key to recognition.

The history should be chronological and describe the evolution of all associated symptoms. While no validated screening tool for secondary headaches currently exists, the mnemonic SNOOP was originally proposed in 2003 and later expanded to SNNOOP10 to provide guidance in this process. The letters in SNNOOP10 represent the following red flags for secondary headaches<sup>6</sup>:

- Systemic features (such as fever, immunocompromise, weight loss)
- Neurologic deficit
- Neoplasm history
- Onset (sudden or new)
- Older age (after 50 years)
- Pattern change
- Positional headache
- Precipitated by Valsalva maneuvers
- Papilledema
- Progressive or atypical
- Pregnancy
- Painful eye with autonomic features
- Posttraumatic onset
- Pathology of the immune system such as HIV
- Painkiller overuse or new medications

Clinicians can use this mnemonic when deciding if the history, examination, and presence or absence of these red flags warrants immediate emergency attention. A headache of sudden onset with rapid escalation to peak intensity (that is, a “thunderclap headache”) should always raise clinical suspicion of a life-threatening event such as a stroke or intracranial hemorrhage.

**Figure 1.** One-Year Prevalence of Migraine by Age and Sex (%)



Reprinted with permission from Finocchi C, Strada L. Sex-related differences in migraine. *Neurol Sci* 2014;35 Suppl 1:207-13.<sup>27</sup>

is not clear. Following migraine resolution, some patients experience a postdrome that may persist up to 48 hours and is commonly characterized by fatigue, difficulty concentrating, and neck pain.

### MIGRAINE PREVALENCE AND DISTRIBUTION

A 2014 review of sex-related differences in migraine found that between the ages of seven and nine, migraine affects the same percentage of boys (2.5%) and girls (2.4%).<sup>27</sup> At puberty, however, the prevalence of migraine in girls markedly increases.<sup>27</sup> (See Figure 1.<sup>27</sup>)

An analysis of age- and sex-specific patterns of migraine prevalence in a U.S. population of 40,892 men, women, and children who participated in the 2003 National Health Interview Survey found migraine prevalence was substantially higher in females (17.5%) than in males (8.6%) from the ages of 10 through adulthood and was highest in both sexes during the reproductive years (from puberty to about age 50).<sup>7</sup> The greatest difference between the sexes occurred between the ages of 20 and 40, when migraine prevalence was 1.5 to 2.9 times higher in women than in men.<sup>7</sup> After age 42, the prevalence remained twice as high in women as in men.

#### Pediatric migraine and associated syndromes.

Diagnosing migraine in children can be difficult because characteristics may be atypical or overlap with other episodic syndromes associated with migraine, which may occur as early as infancy.

*Infantile colic.* The link between migraine and infantile colic, or excessive crying in an otherwise healthy, well-fed infant under the age of four months, was investigated in a prospective study that followed 787 infants from birth through age 18, finding that a history of infantile colic was the only statistically significant predictor of later develop-

ment of migraine without aura, though it was not associated with a risk of migraine with aura, suggesting a genetic difference between migraine with and without aura.<sup>28, 29</sup>

*Benign paroxysmal torticollis* tends to affect older infants and preschool-aged children, with onset occurring at ages five to six months and episodes typically lasting from hours to days, occurring at regular intervals, and usually resolving at ages three to four years.<sup>30</sup>

*Benign paroxysmal vertigo.* Some children with benign paroxysmal torticollis later develop benign paroxysmal vertigo of childhood, with episodes lasting seconds to hours with or without a headache.<sup>30</sup> The condition occasionally persists into adulthood.<sup>30</sup>

*Abdominal migraine* manifests as paroxysmal chronic and recurrent moderate to severe abdominal pain that may be midline, periumbilical, or diffuse in location and is associated with anorexia, nausea, and vomiting.<sup>31</sup> It is one of the most common childhood migraine variants, typically manifesting between the ages of four and seven, though it can occur in children as young as one year and may continue through adulthood.<sup>31</sup> Affected children often have a history of migraine in a first-degree relative.<sup>31</sup> In the absence of headache, such gastrointestinal manifestations may lead to costly and unnecessary testing if clinicians fail to consider the diagnosis of migraine and determine whether there is a family history of migraine.<sup>31</sup>

*Other pediatric syndromes* associated with a family history of migraine include recurrent limb pain, cyclic vomiting, and motion sickness.<sup>31</sup> Pediatric syndromes associated with migraine often cause school absences, difficulty completing assignments, missed family time, and loss of extracurricular and social activities. The associated stress resulting from social isolation, pain, and life disruptions can worsen the migraines.<sup>32</sup>

### MIGRAINE CLASSIFICATION

Migraine is categorized chiefly by the presence or absence of aura, and by aura types, which are subdivided into typical aura (visual, sensory, and/or speech or language), brainstem aura, hemiplegic migraine (when the aura includes motor weakness), or retinal migraine.<sup>4</sup> Within these categories, migraine can be further characterized by the following<sup>4</sup>:

- frequency of the episodes (chronic or episodic)
- specific timing of episodes (as with menstrual migraine)
- complications, such as
  - status migrainosus
  - persistent aura without infarction
  - migrainous infarction
  - migraine aura-triggered seizure

The complete classification criteria are available in the ICHD-3.<sup>4</sup>

**Chronic migraine** is defined as the presence of headache 15 or more days per month for more than three months during which at least eight days per month the headache has migraine features.

**Episodic migraine** is the presence of headache fewer than 15 headache days per month regardless of the number of migraine days.

**Menstrual migraine.** Within the category of episodic migraine, some women have migraines that occur strictly in association with menstruation, ranging from one to two days prior to menses through the cessation of menstrual flow.<sup>4</sup>

### MIGRAINE RISK FACTORS AND COMORBID CONDITIONS

The Migraine in America Symptoms and Treatment Study found migraine to be strongly associated with depression, anxiety, insomnia, asthma, gastric ulcers, diabetes, angina, epilepsy, and inflammatory comorbid conditions such as psoriasis.<sup>10</sup> In North American studies, the prevalence of migraine is inversely related to household socioeconomic status.<sup>33</sup>

Migraine is a risk factor for cardiovascular disease in women under age 50, particularly those who have migraine with aura, which increases their risk of ischemic stroke. The use of estrogen-containing contraceptives is an independent risk factor for ischemic stroke, and stroke risk increases significantly in those who are also cigarette smokers.<sup>34</sup> While the absolute risk of stroke in young women who have migraine with aura and use estrogen-containing hormonal contraception is quite low, this combination of factors requires careful consideration in both the ongoing management and the triage of an acute headache.<sup>35</sup> Nurses should bear in mind the potential risks of estrogen-containing contraceptives when female patients who use these contraceptives and experience migraine with aura report a new type of headache, particularly if the patient is a smoker, and use their judgment in counseling female patients about whether a low-estrogen, monophasic, progestin-only, or nonhormonal contraceptive choice is appropriate.

**Risk factors for migraine progression or chronicity** include the following<sup>36</sup>:

- a high baseline headache frequency
- overuse of medications to control symptoms
- insufficient headache relief and prophylaxis
- female sex
- obesity
- depression
- low socioeconomic status
- stress
- sleep disturbances

When discussing a headache treatment plan with patients, nurses should specifically ask about risk factors, including coexisting disorders, and suggest ways to address modifiable risks.

### NURSING ASSESSMENT OF MIGRAINE

**Signs and symptoms.** Migraine headache is typically a unilateral, throbbing, or pulsing pain of moderate to severe intensity. If untreated or treated ineffectively, episodes may last four to 72 hours in adults and two to 72 hours in children.<sup>4</sup> The pain almost always worsens with physical activity, which is one of the most helpful diagnostic features to obtain in the history. In addition to pain, the migraine is accompanied by nausea, vomiting, photophobia, and phonophobia.<sup>4</sup> A diagnosis of migraine does not require all of the “typical” features, and presentation may vary greatly among patients and between episodes. Additional symptoms may include osmophobia and confusion.

**Imaging and testing.** Migraine is a clinical diagnosis, with no additional laboratory tests or imaging required in most cases. There is no evidence that imaging would reveal any meaningful abnormalities in patients with a typical migraine history and a normal neurologic exam.<sup>37</sup> However, providers should consider imaging or other testing as appropriate in patients who have headaches with unusual historical features, risk factors for progression or chronicity, or headaches that are inconsistent with migraine diagnostic criteria. When imaging is indicated, magnetic resonance imaging is preferred, except in the context of head trauma or to rule out hemorrhage as the cause of an acute headache, in which cases computed tomography should be used.<sup>38</sup>

**Headache history.** A comprehensive headache history is invaluable in determining the correct diagnosis and formulating a comprehensive treatment plan that emphasizes ongoing management. Screening for migraine risk factors and common comorbidities using a validated questionnaire can guide clinicians in developing individualized headache treatment plans. The presence of other medical disorders, such as cardiovascular disease, renal or hepatic dysfunction, asthma, or chronic obstructive pulmonary disease, may preclude the use of certain migraine treatments.

**Follow-up visits.** After a thorough initial history, follow-up visits should assess any changes in headache symptoms and frequency, as patients with migraine may experience several types of headache concurrently. For example, in patients with chronic migraine, the nonmigraine days often meet ICHD-3 criteria for tension-type headache. This can make it difficult for patients to answer questions about their headaches and for nurses to determine the full scope of the patient’s headache burden. To do so, it’s necessary to thoroughly parse out each headache type, which can be incredibly time consuming.

**Headache diary.** To speed this process, we recommend asking patients to start by describing their most debilitating headache type and, after ensuring

they understand the difference between preventive and acute treatments, encouraging them to keep a diary of their headache frequency, symptoms, and severity; acute treatment efficacy; and any adverse effects of medication or barriers to obtaining care. Some patients prefer using a mobile phone app, such as Migraine Buddy (<https://migrainebuddy.com>) for this purpose.

The patient's headache diary should include a list of all headache treatments taken, including both prescribed and over-the-counter medications, as well as any nutraceuticals used for headache. It should note the frequency of each headache treatment and also track caffeine intake, which can increase risk of medication overuse headache (previously termed "rebound headache").<sup>39</sup> Because it may reveal the patient's risk of medication overuse headache, the headache diary is a critical component of the patient history. While some patients report "rebound" after a few days or a week of acute medication use, depending on the medication, this diagnosis requires at least 10 to 15 or more headache days per month for more than three

plan may include a second dose of the first medication or treatment with a secondary medication in a different class.<sup>40</sup> The American Migraine Foundation, however, advises against combining vasoconstrictive drugs—for example, two triptans or a triptan plus ergotamine—within a 24-hour period, and suggests that patients should be alert for signs of serotonin syndrome if combining triptans and either a selective serotonin reuptake inhibitor or a serotonin–norepinephrine reuptake inhibitor.<sup>41</sup>

Remember to address nausea with patients, if necessary, as this is often one of the more debilitating symptoms of migraine.

Therapy is stratified based on migraine-related disability. Acute treatment usually starts with an NSAID, such as ibuprofen, naproxen (Naprosyn and others), diclofenac (Cambia and others), or indomethacin (Indocin, Tivorbex). Before seeking professional medical help, many patients have already tried over-the-counter agents to alleviate symptoms, but NSAIDs can still be useful as monotherapy for milder episodes or in combination with other therapies.

## Most acute medications work best when taken early in the headache process, so patients may need coaching to avoid a 'wait and see' approach.

months of acute treatment.<sup>4</sup> Although opioids and triptans carry the greatest risk of medication overuse headache, any analgesic can bring it on, as can high caffeine intake and tranquilizer use.<sup>39</sup>

### ACUTE MIGRAINE TREATMENT

All patients with migraine should be offered acute treatment. Counseling on the appropriate use and expectations of acute therapies is important for long-term success and adherence. To avoid medication overuse headache, patients should be counseled to limit use of acute medication to no more than 15 days per month for simple analgesics, such as aspirin, nonsteroidal antiinflammatory drugs (NSAIDs), or acetaminophen, and to fewer than 10 days per month for ergotamine (Ergomar), triptans, butalbital-containing compounds, and opioids.<sup>39</sup>

Most acute medications work best when taken early in the headache process, so patients may need coaching to avoid a "wait and see" approach. Uncertainty of pain relief and quantity limits on prescription medication cause significant anxiety for many patients, so it's often beneficial to have a backup plan in case the first dose fails. The backup

**Migraine-specific medications** include the well-established triptan and ergot classes as well as the new ditan and gepant agents.<sup>42</sup>

The triptans target the serotonin receptors 5-HT<sub>1B/1D</sub> and have been a mainstay in migraine therapy for decades.<sup>43</sup> Ergots such as dihydroergotamine (D.H.E. 45 and others) have multiple sites of action. Dihydroergotamine is often effective when patients are unresponsive to triptans and is only available for parenteral and nasal administration. Since both triptans and ergots have vasoconstrictive effects, both are contraindicated in patients with coronary artery disease, cerebrovascular disease, peripheral vascular disease, uncontrolled hypertension, hemiplegic migraine, and migraine with brain-stem aura.<sup>40</sup>

New acute treatment options that avoid cardiovascular and other risks became available in 2020. These include lasmiditan (Reyvow), a serotonin antagonist that binds to the 5-HT<sub>1F</sub> receptor, but unlike triptans does not cause vasoconstriction of coronary arteries, in addition to ubrogepant (Ubrovelvy) and rimegepant (Nurtec ODT), which are small molecule CGRP antagonists that have the

potential to provide an acute treatment with a low risk of medication overuse headache.<sup>42</sup> Rimegepant is also used for preventive treatment.

Barbiturates (such as butalbital) and opioids should not be prescribed routinely for migraine. If a patient has experienced treatment failure or has contraindications to typical migraine treatments discussed above, referral to a neurologist or headache specialist is in order. In addition to the well-known association between opioids and tolerance, addiction, and withdrawal, opioids can cause medication overuse headache with use on fewer than nine days per month.<sup>40</sup>

**External neuromodulation devices** are nonpharmacological treatments employed as either stand-alone or adjunctive acute treatment. They include trigeminal nerve stimulation, noninvasive vagal nerve stimulation, nonpainful remote electrical stimulation, transcranial magnetic stimulation, and a multichannel device incorporating both trigeminal (specifically supraorbital and bilateral supratrochlear) and occipital stimulation. Some are cleared for migraine prevention by the U.S. Food and Drug Administration.<sup>44</sup> In clinical practice, insurance coverage is often limited or unobtainable,<sup>44</sup> so before prescribing these treatments, a frank discussion of their costs and potential benefits is in order.

**To assess patients' responses** to acute therapy, ask when they take their medication during an episode, how long it takes to feel an effect, and how long it takes for complete headache relief. An effective treatment should provide meaningful relief within two to four hours without headache recurrence.

Parenteral forms of ergots, triptans, and antiemetics may be used in combination with an NSAID or an antiemetic when oral preparations are ineffective in relieving moderate to severe migraine symptoms, or in the presence of severe nausea and vomiting.<sup>40</sup>

## PROPHYLACTIC MIGRAINE TREATMENT

Preventive medication is indicated in the following cases<sup>45</sup>:

- when headaches occur on four or more days per month
- when headaches interfere significantly with daily life even when treated acutely
- when acute treatments are contraindicated, fail to provide sufficient relief, or are overused (ergotamine, triptans, butalbital, or opioids used more than 10 days per month or simple analgesics used more than 15 days per month)

Other considerations include the presence of brainstem aura, hemiplegic migraine, migraine with prolonged aura, and history of migrainous infarction.<sup>45</sup>

Selecting the optimal preventive regimen for a patient can be challenging and include factors such as adverse reactions, difficulty with daily adherence, cost, and perceived lack of efficacy. Some degree of

trial and error is typically involved. It's important to provide early patient teaching on potential adverse effects and appropriate expectations. Many oral medications require eight weeks at a target dose to determine effectiveness.<sup>45</sup> Counsel patients who have a partial response that a cumulative benefit may occur in six to 12 months of continued treatment.<sup>45</sup> Migraine is a chronic pain condition and meaningful improvement requires time and patience.

For a list of prophylactic migraine treatments, see Table 2.<sup>46-56</sup>

**Oral medications.** The major classes of oral migraine preventative medications are anticonvulsants, antihypertensives, antidepressants, gepants, and triptans (for menstrual migraine).<sup>57, 58</sup>

In determining the best prophylactic option for a patient, clinicians should consider the following<sup>45</sup>:

- the patient's history
- comorbid conditions
- potential for drug interactions
- contraindications
- personal preferences
- out-of-pocket cost

Multiple agents may be required for intractable cases and often work synergistically, particularly when treating comorbid conditions, such as depression, in addition to headache.<sup>45, 58</sup>

There is no "one size fits all" plan for migraine prophylaxis. Each medication has its own potential pros and cons. For this reason, we suggest that practitioners start by familiarizing themselves with one medication from each class and learn when referral is appropriate. Nutraceuticals that have shown benefit similarly require an adequate trial period at an appropriate dose. These include such supplements as riboflavin, magnesium, and coenzyme Q10.<sup>59</sup>

**Parenteral options.** While generally well tolerated and effective, parenteral options are usually cost-prohibitive without insurance coverage (often requiring treatment failure of two oral medications from different classes).

*The anti-CGRP monoclonal antibodies* emerged on the market in early 2018. These include erenumab (Aimovig), fremanezumab (Ajovy), and galcanezumab (Emgality), which are subcutaneously injected either monthly or quarterly, and eptinezumab (Vyepti), which is administered by IV infusion quarterly.<sup>45</sup>

*Pericranial nerve blocks.* Subcutaneous injections of a lidocaine-dexamethasone solution are minimally invasive, well tolerated, and can provide both prophylactic and acute headache relief.<sup>60</sup>

*OnabotulinumtoxinA (Botox)* is an effective option for chronic migraine. In women who are pregnant or breastfeeding, however, its use should be considered only after a thorough risk-benefit analysis.<sup>45, 61</sup>

**Table 2.** Summary of Prescription Migraine Prophylactic Medications<sup>1, 46-56</sup>

Medication	Adverse Effects	Clinical Considerations and Comments
Anticonvulsants		
Topiramate (Topamax and others)	Paresthesia, decreased appetite and weight loss, cognitive problems (such as word-finding difficulty, slowed thinking, concentration difficulty), taste changes, fatigue, somnolence, mood changes, alopecia, renal calculi, metabolic acidosis, hypokalemia, angle closure glaucoma (idiosyncratic)	<ul style="list-style-type: none"><li>• Beneficial in patients who are overweight or obese, since decreased appetite and weight loss are potential side effects</li><li>• Many adverse effects are dose dependent and responsive to lowering the dose or switching to an extended-release formulation</li><li>• Teratogenic; ensure women of child-bearing potential are using reliable contraception</li><li>• Monitor: creatinine, bicarbonate, electrolytes, ammonia</li><li>• Despite mood changes and possible depression, suicidal thoughts and profound depression are rare</li></ul>
Divalproex sodium (Depakote), sodium valproate <sup>a</sup>	GI disturbance (nausea, vomiting, diarrhea, abdominal discomfort), asthenia, somnolence, weight gain, dizziness, tremor, alopecia, dyscrasias, hepatitis, hyperammonemia, pancreatitis	<ul style="list-style-type: none"><li>• Teratogenic; ensure women of child-bearing potential are using reliable contraception</li><li>• Monitor: liver function tests, CBC, ammonia</li></ul>
Antihypertensives		
β-blockers: atenolol <sup>a</sup> (Tenormin), metoprolol <sup>a</sup> (Lopressor and others), nadolol <sup>a</sup> (Corgard), propranolol, timolol	Cold extremities, fatigue, lightheadedness, dizziness, bradycardia, exercise intolerance, bronchospasm, depression, erectile dysfunction	<ul style="list-style-type: none"><li>• Beneficial in patients with hypertension, essential tremor, anxiety, panic attacks</li><li>• Contraindicated in patients with asthma, congestive heart failure, heart block, peripheral vascular disease; caution with depression, diabetes</li></ul>
Candesartan <sup>a</sup> (Atacand)	Hypotension, orthostatic lightheadedness, congestive heart failure	<ul style="list-style-type: none"><li>• May be beneficial in patients with hypertension who cannot tolerate or did not benefit from a β-blocker</li></ul>
Lisinopril <sup>a</sup> (Prinivil, Zestril)	Cough, dizziness, headache, fatigue, muscle cramps, diarrhea	
Antidepressants		
Amitriptyline <sup>a</sup>	Weight gain, sedation, constipation, dry mouth, blurred vision, sexual dysfunction, orthostatic hypotension, dizziness, cardiac arrhythmia, pancytopenia	<ul style="list-style-type: none"><li>• Beneficial in patients with insomnia, depression, anxiety, acephalic migraine</li><li>• May provoke mania in bipolar disorder</li></ul>
Venlafaxine <sup>a</sup> (Effexor XR)	GI disturbance (nausea, constipation), insomnia, dizziness, anorexia, dry mouth, heat intolerance, excessive sweating, fatigue, sexual dysfunction	<ul style="list-style-type: none"><li>• Beneficial in patients with depression or anxiety</li><li>• Less likely to cause sedation and weight gain than amitriptyline</li><li>• Has a prominent withdrawal syndrome; warn patients against sudden discontinuation</li></ul>
Triptans (for short-term prophylaxis of menstrual migraine)		
Frovatriptan <sup>b</sup> (Frova), naratriptan <sup>b</sup> (Amerge), zolmitriptan <sup>b</sup> (Zomig)	Dizziness, fatigue, paresthesia, headache, vascular flushing	<ul style="list-style-type: none"><li>• Generally well-tolerated compared to other triptans</li><li>• Contraindicated in patients with ischemic cardiovascular disease, uncontrolled hypertension, hemiplegic and basilar migraine (brain-stem aura)</li></ul>

(continued)

**Table 2.** Continued

Injectable agents		
OnabotulinumtoxinA (Botox)	Neck pain, muscle weakness, ptosis, injection-site pain, musculoskeletal pain	<ul style="list-style-type: none"> <li>• Multiple treatments may be required before seeing benefit; warn patients prior to initiating therapy that patience is required</li> <li>• Good safety and tolerability profile</li> <li>• Only approved for treatment of chronic migraine; prior authorization often requires treatment failure or contraindication to two oral preventive agents</li> </ul>
CGRP monoclonal antibodies: eptinezumab (Vyepti), erenumab (Aimovig), fremanezumab (Ajovy), galcanezumab (Emgality)	Injection-site reaction or pain, nasopharyngitis or upper respiratory infection, constipation (rarely ileus), alopecia	<ul style="list-style-type: none"> <li>• Good safety and tolerability profile</li> <li>• Available as self-administered subcutaneous injection (erenumab, fremanezumab, galcanezumab) or IV infusion (eptinezumab)</li> <li>• Prior authorization often requires treatment failure or contraindication to two oral preventive agents</li> </ul>
Oral CGRP antagonists		
Rimegepant (Nurtec ODT)	Nausea, dyspepsia, hypersensitivity reactions including dyspnea and rash	<ul style="list-style-type: none"> <li>• Avoid with strong or moderate CYP3A4 inhibitors, strong or moderate CYP3A inducers, or P-gp or BCRP inhibitors. Avoid in patients with end-stage renal disease or severe hepatic impairment</li> <li>• Effect in pregnancy and lactation unknown</li> <li>• Good safety and tolerability profile</li> <li>• CGRP antagonists with shorter half-life than CGRP monoclonal antibodies, allow for rapid clearance if needed</li> <li>• Prior authorization often requires treatment failure or contraindication to two oral preventive agents</li> </ul>
Atogepant (Qulipta)	Nausea, constipation, fatigue	<ul style="list-style-type: none"> <li>• Reduce dose with strong CYP3A4 inhibitors, strong or moderate CYP3A4 inducers, OATP inhibitors, severe hepatic impairment, severe or end-stage renal disease</li> </ul>

BCRP = breast cancer resistance protein; CBC = complete blood count; CGRP = calcitonin gene-related peptide; CYP = cytochrome P-450; GI = gastrointestinal; OATP = organic anion transporting polypeptide; P-gp = P-glycoprotein.

<sup>a</sup> Off-label use for migraine.

<sup>b</sup> Off-label use for menstrual migraine prophylaxis but on-label use for migraine headache.

**Pure menstrual migraine**, in which episodes occur strictly during menstruation or one to two days prior, requires a unique approach to prevention. In addition to prophylactic therapies, menstrual migraine can be treated with “mini-prophylaxis” using a long-acting triptan, such as frovatriptan (Frova), naratriptan (Amerge), or zolmitriptan (Zomig), on a daily basis, as well as naproxen or magnesium.<sup>62</sup> Medication overuse is generally not an issue in this context, as the duration of use is limited and predictable because few women have menstrual periods exceeding 10 days per month, which is the lower limit of triptan use for medical overuse criteria.

### LIFESTYLE MODIFICATIONS AND NONMEDICINAL MIGRAINE THERAPY

In addition to counseling patients on medication management, lifestyle modifications, diet, and trigger tracking, encourage patients to take an active role in their pain management by following consistent and adequate sleep–wake schedules and looking for ways to reduce and manage stress. While worsened pain with physical activity is common during a migraine episode, studies suggest that routine exercise may increase levels of  $\beta$ -endorphins and decrease headache frequency and duration over time.<sup>63</sup> With the use of a symptom and diet diary, patients can develop a sense of self-efficacy by identifying patterns

and avoiding consistent food triggers. Skipping meals or dehydration are common but easily avoided pitfalls. Common dietary triggers include caffeine (especially withdrawal), artificial sweeteners, alcohol, and aged or smoked meats and cheeses. While dietary triggers have been said to include gluten, histamine, tyramine, sulfites, and monosodium glutamate, studies of elimination diets have been inconsistent, and no specific elimination diet can be recommended for most migraine patients.<sup>63</sup>

Nonmedicinal acute headache treatments may help patients avoid medication overuse headache. Acute migraine episodes often benefit from rest and relaxation in a dark, quiet place; thermal and electromyographic biofeedback; and cognitive behavioral therapy focused on stress management, relaxation strategies, biofeedback, and mindfulness therapies that help patients control stress-related autonomic arousal and learn skills for coping with chronic pain conditions.<sup>59</sup> ▼

For 12 additional nursing continuing professional development activities on the topic of migraine, go to [www.nursingcenter.com](http://www.nursingcenter.com).

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