Headache is one of the chief complaints among patients visiting primary care physicians. Diagnosis begins with exclusion of secondary causes for headache. More than 90% of patients will have a primary-type headache, so diagnosis can often be completed without further testing. Although tension-type headaches are the most common kind of headache, patients with this type of headache rarely seek treatment unless occurrence is daily. Migraine, which affects more than 30 million people in the United States, is the most common headache diagnosis for which patients seek treatment. Migraine is a chronic, often inherited condition involving brain hypersensitivity and a lowered threshold for trigeminal-vascular activation. Intermittent debilitating attacks are characterized by autonomic, gastrointestinal, and neurologic symptoms. Migraine results in a marked decrease in a patient’s quality of life, as measured by physical, mental, and social health-related instruments. Accurate assessment of a patient’s disability will guide physicians in prescribing appropriate modes of therapy. However, migraine remains underdiagnosed, and patients with migraine remain undertreated.

A comprehensive treatment approach to migraine may include nonpharmacologic measures, as well as abortive and prophylactic medications. Informing patients about realistic treatment expectations, possible delayed efficacy of medications, and avoidance of caffeine and overuse of medications is critical for successful outcomes. Management of migraine is a dynamic process, because headaches evolve over time and medication tachyphylaxis may occur, necessitating changes in therapy. Pathologic findings in the neck constitute an accepted etiology for headaches. 4 The diagnosis for these headaches evolve over time and medication tachyphylaxis may occur, necessitating changes in therapy. Pathologic findings in the neck constitute an accepted etiology for headaches. 4 The diagnosis for these headaches evolve over time and medication tachyphylaxis may occur, necessitating changes in therapy. Pathologic findings in the neck constitute an accepted etiology for headaches. 4 The diagnosis for these headaches evolve over time and medication tachyphylaxis may occur, necessitating changes in therapy. Pathologic findings in the neck constitute an accepted etiology for headaches. 4 The diagnosis for these headaches evolve over time and medication tachyphylaxis may occur, necessitating changes in therapy. Pathologic findings in the neck constitute an accepted etiology for headaches. 4 The diagnosis for these headaches evolve over time and medication tachyphylaxis may occur, necessitating changes in therapy. Pathologic findings in the neck constitute an accepted etiology for headaches. 4 The diagnosis for these headaches evolve over time and medication tachyphylaxis may occur, necessitating changes in therapy. Pathologic findings in the neck constitute an accepted etiology for headaches. 4 The diagnosis for these headaches evolve over time and medication tachyphylaxis may occur, necessitating changes in therapy. Pathologic findings in the neck constitute an accepted etiology for headaches. 4 The diagnosis for these headaches evolve over time and medication tachyphylaxis may occur, necessitating changes in therapy. Pathologic findings in the neck constitute an accepted etiology for headaches. 4 The diagnosis for these headaches evolve over time and medication tachyphylaxis may occur, necessitating changes in therapy. Pathologic findings in the neck constitute an accepted etiology for headaches. 4 The diagnosis for these headaches evolve over time and medication tachyphylaxis may occur, necessitating changes in therapy. Pathologic findings in the neck constitute an accepted etiology for headaches. 4 The diagnosis for these headaches evolve over time and medication tachyphylaxis may occur, necessitating changes in therapy. Pathologic findings in the neck constitute an accepted etiology for headaches. 

Migraine is a common condition, annually affecting 12% of the United States population, including 18% of women, 6% of men, and 4% of children. 1,3 Lifetime prevalence of migraine in women in the United States exceeds 25%. 1,3 The prevalence of migraine has not changed since 1989, based on evidence from three large studies: American Migraine Study I, 1 American Migraine Study II, 2 and American Migraine Prevention and Prevalence Study. 3 Migraine in the United States is more prevalent in Caucasians than in African Americans, and the lowest prevalence in the United States is among Asian Americans. 2 Migraine is generally more common in people who are in lower socioeconomic groups. 2

Migraine typically begins affecting individuals when they are in their teens or twenties, with peak prevalence occurring at approximately age 40 years. 2 First onset of migraine after age 50 years should raise suspicion of secondary headache causes. One quarter of adults with migraine will experience four or more severe attacks per month, each with a mean duration of about 24 hours. 2

**Diagnosis of Migraine**

Migraine is a diagnosis strongly linked to a patient’s medical history. Typical characteristics of migraine headache include unilateral throbbing pain associated with moderate to severe disability, nausea, vomiting, phonophobia, photophobia, and increased pain with physical exertion. 4 Migraine in children is generally shorter in duration than migraine in adults, with less pronounced associated symptoms and possible presentation as cyclic vomiting, abdominal symptoms, or paroxysmal vertigo rather than head pain. 4

It is important to note that no isolated characteristic is necessary to make the diagnosis of migraine. The three most predictive characteristics for a migraine diagnosis are disability, nausea, and photophobia. 5 An abbreviated set of diagnostic criteria for migraine is available in a validated screening instrument called ID Migraine. 5

Less than a third of patients with migraine have focal neurologic signs, termed auras, just before or during some headaches. 4 The diagnosis for these patients is migraine with aura (formerly called “classic migraine”), in contrast to
Migraine without aura (formerly called “common migraine”). Auras are most commonly visual and less commonly sensory or motor in nature. Migraines associated with motor auras are called hemiplegic migraines and may occur on a hereditary basis within families and a sporadic basis among individuals. Trip-tans are contraindicated for patients with hemiplegic migraine because of a lack of adequate testing of these medications in this small population.

Migraine is often mistaken for sinus or tension headache. Migraine is confused with sinus headaches because the autonomic symptoms of migraine include nasal stuffiness or discharge, occurring in 87% of patients with migraine. In addition, the headache in these patients may be located above the sinuses. Migraine often is confused with tension headache because 75% of patients with migraine have neck pain during or immediately before or after a migraine.

The diagnosis of migraine is based on criteria developed by the International Headache Society in 1988 and revised by the society in 2004—the International Classification of Headache Disorders II (ICHD II). Similar to the Diagnostic and Statistical Manual of Mental Disorders (DSM IV) used in psychiatric evaluations, the ICHD II requires that patients’ headaches must have certain characteristics for each kind of diagnosis (Figures 1 and 2). Headaches are categorized by primary or secondary headaches, with four broad groups of primary headaches, including migraine, tension, cluster, and miscellaneous headaches, and 10 broad groups of secondary headaches (Figure 2).

Although necessary for medical research, the ICHD II criteria may be cumbersome for use by physicians in the primary care setting. Nevertheless, the criteria do offer a process for organizing a differential diagnosis; if patients have the symptoms listed in the criteria, physicians are more comfortable that the patient truly has that primary headache diagnosis and is less likely to have a brain tumor or other grave condition.

Any abnormalities in a patient’s medical history or physical examination suggesting secondary headache must be carefully evaluated before making a primary headache diagnosis. However, recommendations by the US Headache Consortium state that neuroimaging is generally not necessary in adult patients presenting with typical migraine, normal findings on neurologic examination, and no recent change in headache characteristics. These recommendations are based on data indicating that only 0.18% of this patient group show a clinically significant intracranial pathologic lesion on neuroimaging.

Triggers of Migraine
Migraine is believed to be an inherited condition of cortical hyperexcitability. Some patients with migraine are able to identify headache triggers. Triggers may be inconsistent or additive and are not specific to migraine. For example, menses is a trigger for 60% of female migraineurs and is also a trigger for tension-type headache. Stress or “let-down” after a stressful event, change in sleep or meal schedules, and such environmental factors as loud noise, odors, or flickering lights may also precipitate migraine headache.

Approximately a quarter of patients with migraine recognize certain food as migraine triggers. Such triggers include monosodium glutamate (also known as hydrolyzed yeast extract, natural flavoring, hydrolyzed vegetable protein), often found in soups and Chinese food. Nitrites (a preservative found in lunch meats and hot dogs), tyramines (found in wines and such aged foods as cheeses), and phenylethylamine (found in chocolate, garlic, nuts, raw onions, and seeds) are other potential migraine triggers. Alcohol of any kind, artificial sweeteners, citrus fruits, pickled products, and vinegars are additional likely triggers. It should be noted that not all patients have these food triggers, so a diet totally eliminating these items is not warranted in all migraineurs.

Daily consumption of caffeine can lead to caffeine withdrawal headaches or rebound headaches interfering with or negating the effects of migraine preventive medications. Daily caffeine consumption is much greater than many people expect, with a typical cup (8 oz) of drip coffee containing about 135 mg of caffeine. Patients should be advised that caffeine is used in combination with many over-the-counter (OTC) pain medications because it enhances analgesia. Caffeine has a half-life of up to 9.5 hours; and the body transforms it into more than 25 metabolites.

Overuse of caffeine is a risk factor for progression of occasional migraine to a chronic daily pattern. Additional considerations for such a progression include acute medication overuse, depression, obesity, sleep disorders, and stressful life events. Head trauma may cause or exacerbate headaches. Based on ICHD II criteria, new onset of headaches within 7 days of head trauma is diagnosed as posttraumatic headache, while continued headache after 3 months is termed
chronic posttraumatic headache. Even mild head trauma without loss of consciousness or objective findings can cause new onset or exacerbation of headaches, necessitating long-term management.4

The proposed neurophysiologic basis for cervicogenic headache is nociceptive input from trigeminal and cervical (C1-C3) afferent neurons converging on second-order neurons in the trigeminocervical nucleus.17 In addition, several recent anatomic discoveries identify direct neuronal connections between extracranial structures and the dura mater.18 Hack et al19 found a neuronal connection between the rectus capitis posterior minor muscle and dorsal spinal dura mater at the atlanto-occipital junction, which appears to restrict dural movement toward the spinal cord. Abnormalities in the cervical spine, such as muscular spasm, may transmit forces to the pain-sensitive dura mater.

Theoretically, alleviating accessible causes of pain through such modalities as osteopathic manipulative treatment (OMT) should increase a patient’s headache thresholds. However, because of a lack of controlled studies on OMT and other modalities, biofeedback is the only nonpharmacologic therapy for migraine that is considered to be “evidence-based” by the US Headache Consortium.8

Pharmacologic Management of Migraine
Abortive Medications

More than 90% of patients with migraine have disability with their attacks, and half these patients require bed rest.20 Despite this high level of disability, less than 60% of patients with migraine have their headache diagnosed as such by a physician.20 Thus, many patients are not adequately treated with abortive or prophylactic medications for migraine. A major obstacle in diagnosing headache in a primary care setting is time constraint. An average office visit by a patient to a primary care physician lasts 9 minutes and usually addresses multiple complaints.2 Scheduling additional visits specifically to address the headache complaint and having patients keep diaries of headache frequency, severity, and medications may help overcome obstacles to proper diagnosis and treatment.

Patients are usually not adept at initiating accurate descriptions of disability experienced during migraine attacks, and physicians may not accurately assess migraine-related disability of their patients, many of whom may be healthy young individuals between headache attacks. In light of these problems, a clinically useful, validated instrument for disability assessment is the Migraine Disability Assessment (MIDAS) tool,21 which can be used to assess the number of work or school days lost during a 3-month period due to migraine. Studies show that healthcare providers are more likely to treat patients with effective, migraine-specific therapeutic modalities if they are aware of the patients’ migraine disabilities.22,23 The Disability in Strategies of Care (DISC) trial22 confirmed that patients with moderate to severe migraine-caused disability are more likely to respond to high-end modes of therapy. In the DISC trial, 75% of patients had a failed response to high-dose aspirin (800-1000 mg/d) and metoclopramide (10 mg/d) therapy, requiring zolmitriptan (2.5 mg/d) as effective high-end therapy.

The US Headache Consortium recommends serotonin 5HT1B/D agonists (ie, triptans) as first-line therapy in a strat-
ified-care approach for patients with migraine who experience moderate to severe disability (Figure 3). Seven triptans are available for migraine, all in tablet formulation. Two of these triptans (rizatriptan, zolmitriptan) are available as oral wafers that may be taken without water; two (sumatriptan, zolmitriptan) are available as nasal sprays; and one (sumatriptan) is available in a subcutaneous formulation. Headache relief with triptans is not pathognomonic to migraine; migraine, tension-type, and secondary headaches may all respond to these drugs. Conversely, not all migraines respond to triptans.

Triptans have the same contraindications in patients with known or suspected ischemic cardiac, cerebrovascular, peripheral vascular, or uncontrolled hypertensive disease. However, the Triptan Cardiovascular Safety Expert Panel concluded that chest symptoms occurring with triptan use are generally not serious or ischemic; the incidence of serious cardiovascular events with triptan use appears to be extremely low; and the cardiovascular risk-benefit profile of triptans favors their use in the absence of contraindications. One type of triptan should not be combined with another type or with a vasoconstrictor within 24 hours of administration. Rizatriptan, sumatriptan, and zolmitriptan should not be used within 2 weeks of administration of a monoamine oxidase (MAO) inhibitor; rizatriptan should be dosed at 5 mg per dose for patients using propranolol hydrochloride; and eletriptan should not be used within 3 days of the use of strong cytochrome P4503A inhibitors, such as clarithromycin.

Labels on all triptans carry a cautionary statement noting that these drugs may cause the “serotonin syndrome” when used in combination with other serotonergic drugs such as serotonin reuptake inhibitors (SSRIs, including the antidepressant fluoxetine hydrochloride; and eletriptan should not be used within 3 days of the use of strong cytochrome P4503A inhibitors, such as clarithromycin.

Interpatient variability also exists for triptan efficacy, with different patients responding differently to particular triptans, and some patients requiring transition from one triptan to another to maintain efficacy. Assessment of efficacy of triptans and other abortive medications should be repeated at each patient visit, with several questions asked of patients and various target endpoints addressed (Figure 4).

Alternative abortive medications to triptans include ergots and their synthetic derivative, dihydroergotamine; butalbital-containing analgesics or other analgesic combinations; isomethypencumate combination; nonsteroidal anti-inflammatory drugs (NSAIDs); and opioids. Administration of butalbital-containing products is controversial because there are no placebo-controlled trials supporting their efficacy for migraine. In addition, the potential exists for butalbital overuse resulting in rebound headaches, and some patients may use butalbital-containing products to treat underlying comorbid anxiety. Opioid therapy is also controversial, with several studies reporting activation of pronociceptive mechanisms with long-term use of opioids.

“Rescue” treatment options when first-line agents fail in an outpatient or emergency department setting include the following: dihydroergotamine, divalproex sodium, droperidol, intranasal lidocaine, ketorolac, magnesium sulfate, opioids, parenteral sumatriptan, prochlorperazine, propofol, and steroids. All of these medications except sumatriptan and dihydroergotamine are used off-label for migraine.

Abortive polytherapy is an option when single agents do not provide adequate relief for patients with migraine. An NSAID and/or a gastrokinetic drug (eg, metoclopramide) may be used in addition to a triptan.

Researchers have found that cutaneous allodynia (a condition in which such nonnoxious stimuli as mechanical pressure and thermal changes cause skin pain) develops in nearly 80% of patients with migraine. Studies indicate that cutaneous allodynia is a marker for central sensitization and abortive medications are less likely to produce complete pain relief after this phenomenon develops.

Providing abortive treatment during the early mild phase of migraine results
in higher pain-free rates among patients. However, for patients with frequent headaches who consistently require treatment more than 2 days per week, prophylactic medication may be needed to reduce headache frequency. The potential for headache rebound exists with frequent use of most abortive medications, including butalbital-combination products, caffeine-containing medications, including butalbital-combination products, caffeine-containing products, and triptans.

Prophylactic Medications

Generally, prophylactic medications (Figure 3) are taken daily to reduce headache frequency, decrease headache intensity, and/or allow for improved abortive management of migraine. However, more subtle improvements in quality of life may warrant continuation of prophylactic therapy, even if a high level of headache reduction is not achieved. Serial MIDAS tests can monitor improvements for such measures as lost work or school days and loss of productivity related to home chores or social functions. More than one prophylactic medication may be used in combination when only a partial response is achieved with one drug and when that drug’s dosage cannot be increased because of maximal dose or drug intolerance. Prophylactic modes of therapy may be used intermittently for headaches occurring at predictable times, such as during menses, exercise, or sexual activity.

Physicians should keep in mind that prophylactic medications are not a cure for headache, and abortive therapy will remain necessary for breakthrough attacks. In addition, patient education about medication use is important for compliance.

No prophylactic medication was originally developed to treat patients with migraine, and only four medications have US Food and Drug Administration (FDA) indication for migraine: divalproex sodium, propranolol, timolol maleate, and topiramate. Major classes of prophylactic medications for migraine include antiepileptics, β-blockers, calcium-channel blockers, and tricyclic antidepressants (Figure 3). The exact physiologic mechanisms of these varied drugs are not known, but the mechanisms are believed to involve suppression of central hyperexcitability and/or enhancement of antinoceptive pathways.

Comorbidities (eg, angina, depression, epilepsy) generally will influence prescribing considerations for prophylactic medications (Figure 3). The US Headache Consortium has published evidence-based guidelines for selecting a prophylactic medication for patients with migraine. There are conflicting reports regarding the efficacy of botulinum toxin A for migraine or chronic daily headache prophylaxis, with most studies not achieving primary endpoint efficacy.

For patients with infrequent migraines and those who are reluctant or unable to use prescription prophylactic medications, alternative agents may be considered. Dietary supplements that may be effective for migraine prevention, based on results of placebo-controlled trials, include butterbur root (Petasites hybridus), coenzyme Q10, feverfew, magnesium, melatonin, and riboflavin (vitamin B2). Many combination products are available, such as MigreLief (feverfew, magnesium, riboflavin) and Migravent (butterbur root, feverfew, magnesium, riboflavin; Vita Sciences, Airmont, NY).

The following anecdotal case presentation describes a typical patient whose case illustrates the diagnosis and management of migraine.

Case Presentation

Cheryl is a 44-year-old woman with perimenopausal symptoms of hot flashes interrupting sleep. She is seen by her physician because of an exacerbation of headaches that are unilateral, hemicranial, throbbing, and associated with nausea and photophobia. At times she must lie in a dark quiet room to try to help ease her headache pain. She denies having associated neurologic symptoms such as vision loss, but she says that she often yawns for several hours before headaches, and she has some nasal congestion and neck ache during the pain phase.

Cheryl’s headaches started at age 14 years, typically occurring only during her menses and persisting for 1 day. She now complains of a gradual increase in headache frequency and duration during the previous 2 years, with her typical “bad” headaches (ie, migraine without aura) occurring both during menses (lasting 4 days) and outside of menses (two attacks lasting 1 day each). Sumatriptan succinate tablets (100 mg/d) no longer provide her with adequate relief.

On further questioning, Cheryl admits to milder headaches occurring on a daily basis for at least the entire previous year. She says she manages those headaches daily with six OTC combination analgesics containing caffeine, accounting for 390 mg of caffeine (65 mg/tablet) per day. She had not initially

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**Table 1.** Factors to assess and target endpoints for assessment of efficacy of abortive medications in treatment of patients with migraine.

<table>
<thead>
<tr>
<th>Factor to Assess</th>
<th>Target Endpoint</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rapidity of relief</td>
<td>Meaningful onset within 1 h</td>
</tr>
<tr>
<td>Partial vs total pain relief</td>
<td>Total relief within 2 h</td>
</tr>
<tr>
<td>Relief of associated symptoms</td>
<td>No nausea, vomiting, photophobia, phonophobia</td>
</tr>
<tr>
<td>Return to normal function</td>
<td>2 h without sedation</td>
</tr>
<tr>
<td>Headache recurrence</td>
<td>Total relief with 1 dose of abortive medication</td>
</tr>
<tr>
<td>Consistency of response</td>
<td>Relief for every headache</td>
</tr>
<tr>
<td>Adverse effects</td>
<td>None or minimal</td>
</tr>
<tr>
<td>Preference/convenience of formulation</td>
<td>Ease of use, taste, convenience</td>
</tr>
<tr>
<td>Cost</td>
<td>Weigh cost against efficacy and function</td>
</tr>
</tbody>
</table>

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**Figure 3.** Prophylactic medications in treatment of patients with migraine.

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**Figure 4.** Factors to assess and target endpoints for assessment of efficacy of abortive medications in treatment of patients with migraine.
Management of Cheryl’s Headaches

Make the Proper Diagnosis—Take a detailed headache history of the patient, including all prescription and OTC medications used and the frequency of their use.

Cheryl’s headache diagnosis is migraine without aura, in addition to probable medication overuse headache. She has a long history of typical migraines. However, the character of her headaches has changed. They have become more frequent and more difficult to manage, requiring additional medications. These changes may indicate the need for further testing, such as brain MRI, though there are certain known reasons for escalation of Cheryl’s headaches.

She is oversusing caffeine and analgesics, substances that may cause, worsen, or maintain her daily headache pattern. She is also premenopausal, with hormonal fluctuations and sleep disturbance. Thus, it may be reasonable to withdraw the oversused agents with close follow-up before conducting further testing.

Educate the Patient About Non-pharmacologic Management—Cheryl should understand that her diagnosis is migraine, that there are no objective markers for this disorder, and that it is usually inherited, chronic, and biochemical in nature.

There is no single definitive cause of migraine or definitive treatment for patients with migraine. However, the disorder can be successfully managed. It is important for the patient to stay regimented in her daily schedule, including meals and sleep. Fluid intake should be maintained, because dehydration is a trigger for migraine. Any identified food triggers for migraine should be avoided, though food may not consistently trigger headaches and may be additive with other stimuli.

The patient should be especially careful to avoid migraine triggers during her most vulnerable time for headaches (ie, during menses). Regular exercise may have beneficial effects on headaches. Relaxation activities, including biofeedback training, listening to relaxation tapes, and performing yoga, may also be beneficial. Furthermore, OMT for paravertebral cervical spasm associated with headaches may be beneficial—though some patients have cutaneous allodynia during acute migraine and may prefer not to be touched at such times.

Have the Patient Follow Up—Headaches change with time, and secondary headaches may develop in patients who have had life-long headaches. In addition, abortive and prophylactic medications need to be continually assessed and adjusted to achieve maximal benefit. Physicians should review headache diaries, any medication adverse effects, and any changes in medical condition that may warrant changes in therapy. Generally, prophylactic medications are continued for approximately 6 months if a beneficial response is achieved, then attempts are made to wean the patient away from the medications.

Prophylactic medications may be stopped with continued observed benefits, or headaches may worsen. If headaches worsen, the lowest dose that adequately controls headache should be maintained.

Cheryl had severe headaches during the first week she was off caffeine and the acetaminophen-ASA-caffeine formulation. She then noticed a lessening of headache intensity, with some headache-free days by the third week of therapy. At her next visit, 1 month later, amitriptyline was increased to 40 mg/d. Two months after her second visit, Cheryl had only one migraine with menses per month. The use of her triptan during these episodes provided complete pain relief within 2 hours. Recurrence of headache 24 hours later was again relieved with her triptan. After 2 months, Cheryl rarely had mild tension-type headaches and did not require abortive treatment for such headaches.

Comment
Migraine is the most common type of headache seen in primary care. Yet, migraine is often not properly diagnosed, and patients with migraine are often
inadequately treated because of physician time constraints, lack of physician understanding of migraine-related disabilities, incorrect patient self-diagnosis, and/or incomplete patient medication history.

Successful management of migraine requires intensive patient education and thorough physician knowledge about available treatment options and strategies. These treatment options and strategies include stratified care with a migraine-specific abortive medication for patients with moderate to severe disability; early intervention with an abortive medication before central sensitization occurs; and the use of a prophylactic medication to reduce headache frequency, severity, and risk for rebound.

References

Editor’s Note
Physicians are advised to check the full prescribing information for all the medications discussed in this article and keep current with all FDA advisories and warnings.