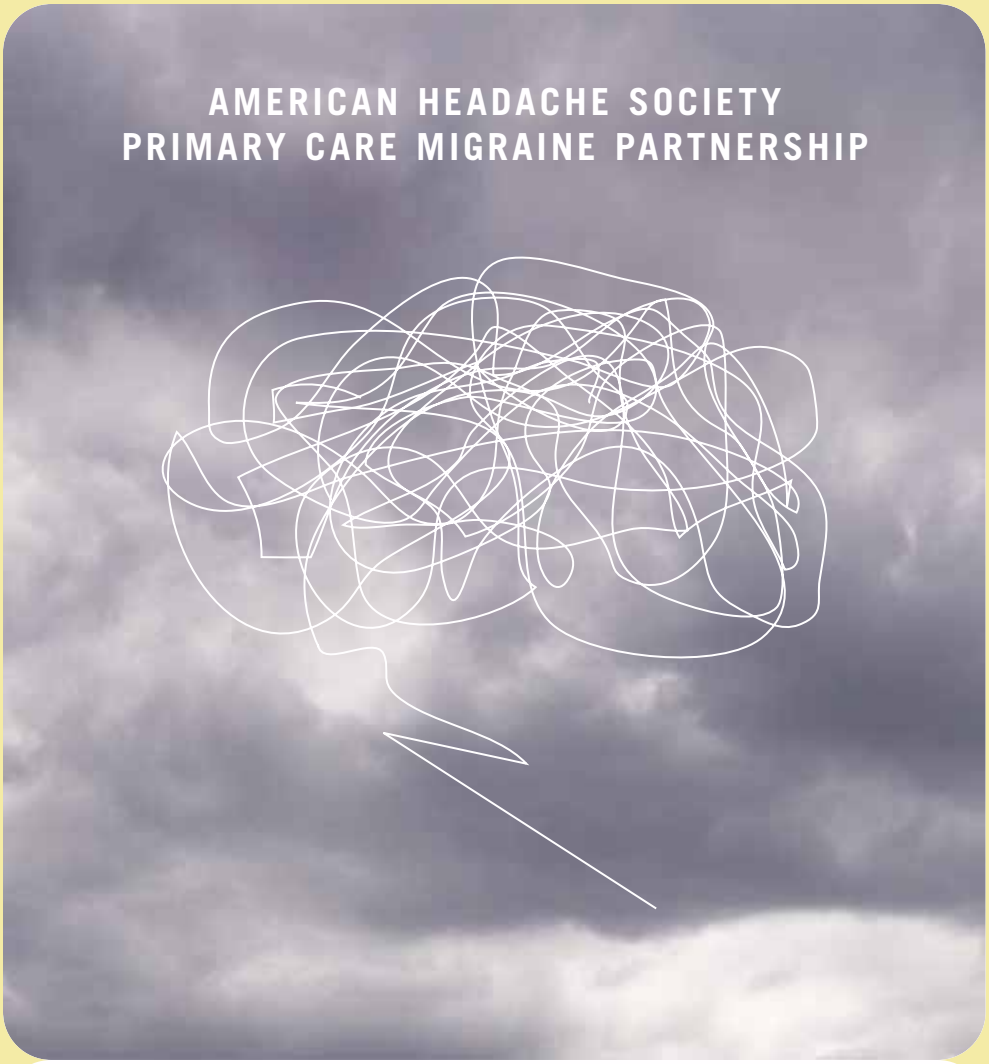

BRAINSTORM

A CME-ACCREDITED COLLABORATIVE SYMPOSIUM
ON DIAGNOSING AND TREATING MIGRAINE

AHS
American Headache Society

Contents

BRAINSTORM

PRIMARY CARE MIGRAINE PARTNERSHIP

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Introduction

The American Headache Society (AHS) welcomes you to Brainstorm—The Primary Care Migraine Partnership's collaborative, interactive educational program. The Primary Care Migraine Partnership is an innovative educational program designed by primary care physicians and neurologists for primary care physicians. This dynamic program results from an extensive needs assessment, including a comprehensive review of the primary care literature and more than 80 hours of interviews with primary care physicians regarding the challenges faced in treating migraine patients. To make Brainstorm possible, 18 primary care and neurologist thought leaders on migraine met to review the information that had been collected and design key educational messages. From this effort, a smaller team of dedicated primary care and headache specialist curriculum developers fashioned this exciting program. Together, we're going to explore the many dimensions of migraine through an interactive, patient-oriented, case-based program. Our goal is to give you practical tools to diagnose and treat migraine while ruling out worrisome headaches.

We would like to thank the industry supporters who have provided unrestricted educational grants to underwrite the development of this program, including:

Abbott Neuroscience · AstraZeneca · Bristol-Myers Squibb Company · MERCK · ORTHO-McNEIL PHARMACEUTICAL, INC. · Pfizer

Continuing Medical Education Credit

ACCREDITATION STATEMENT

This activity has been planned and implemented in accordance with the Essential Areas and Policies of the Accreditation Council for Continuing Medical Education (ACCME) by the American Headache Society (AHS). The AHS is accredited by the ACCME to provide continuing medical education to physicians. The AHS takes responsibility for the content, quality, and scientific integrity of this CME activity.

AMA PRA

The AHS designates this educational activity for a maximum of 2 hours of category 1 credit toward the AMA Physician's Recognition Award (PRA). Each physician should claim only those hours that he/she actually spent in the educational activity.

AAFP

This activity has been reviewed and approved for 2 Prescribed credit hours by the American Academy of Family Physicians (AAFP).

LEARNING OBJECTIVES

At the conclusion of this program, participants will be able to

- Improve accuracy of headache diagnoses in clinical practice
- Understand the pathophysiology of migraine and the mechanisms of drug treatment
- Increase familiarity with standard and new treatments for headache

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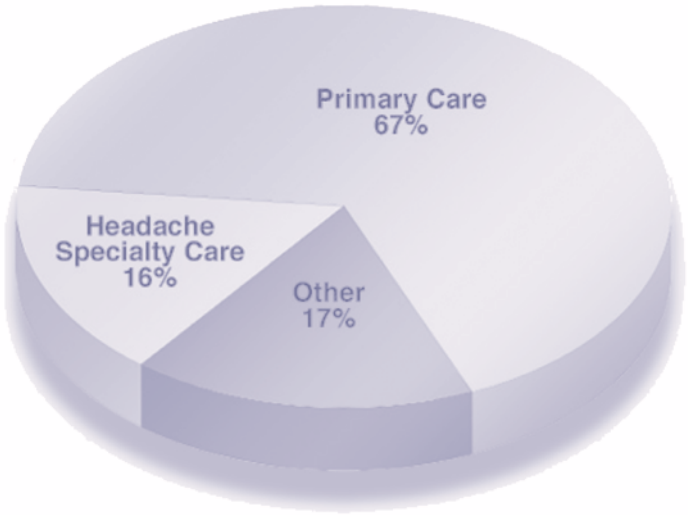
Module 1

Prevalence and Impact of Migraine

Migraine is a common disorder affecting approximately 18% of women and 6% of men. Overall, estimates are that 28 million Americans are migraine sufferers. During childhood, migraine prevalence is similar among boys and girls, but with onset of puberty, the prevalence of migraine increases significantly in women. Unfortunately for patients, migraine prevalence is highest during midlife, a time of peak responsibilities.

Who provides the majority of migraine care? More than two thirds of sufferers are managed in a primary care setting. A recent study showed that about one third of patients in the typical waiting room of a primary care physician are migraine sufferers. This tells us that many migraine sufferers seek medical care but may not do so specifically for migraine. Another way to look at the prevalence of migraine is to consider that approximately one in four households in America has a family member with migraine. The fact that migraine is so common and disabling points to the need for primary care physicians to provide routine screening for the condition as part of overall patient care.

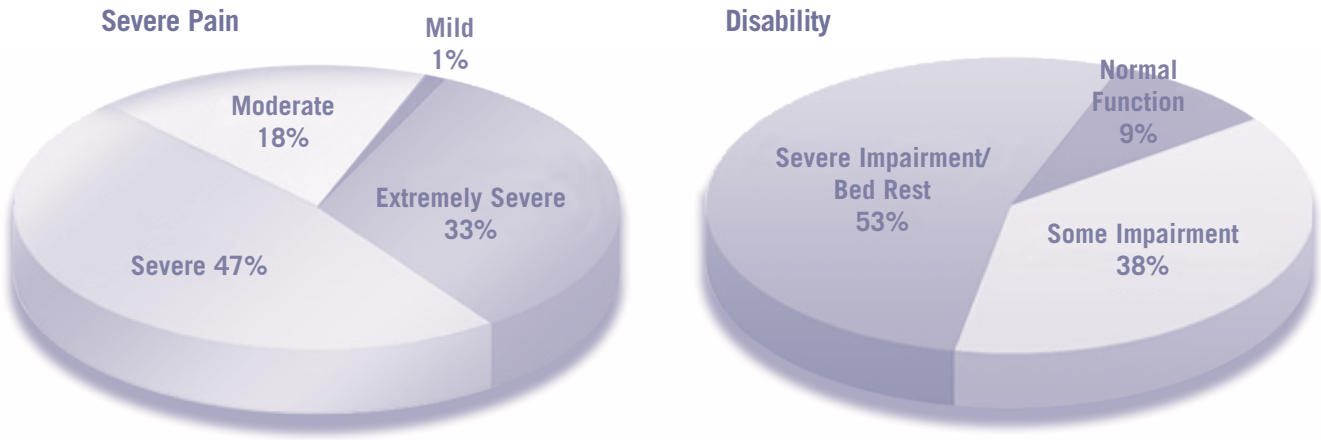
Where Do Migraine Sufferers Seek Medical Care?



Lipton RB et al. *Headache.* 1998;38:87-96.

Why is it important to identify migraine sufferers in the primary care setting? Migraine is an illness of long duration that causes episodic attacks of severe headache and associated neurologic symptoms such as nausea, vomiting, photophobia, dizziness, cognitive impairment, and lethargy. Many patients are unable to work, or their work productivity is reduced during and between attacks. The impact of migraine is evident not only in the workplace, but also on family life, relationships with spouses, quality of life, and overall well-being. Conservative estimates are that migraine costs Americans $13 billion annually.

Migraine Patients Experience Severe Pain and Disability



Lipton RB et al. *Headache.* 2001;41:638-645.

Health expenditures for migraine patients are higher than those for nonmigraineurs. This is true not only for headache-related expenditures, but also for treatment of coexisting conditions such as depression or anxiety. Recognition and appropriate management of migraine can translate into:

- Fewer routine telephone calls/urgent office visits
- Fewer emergency department visits and hospitalizations
- Reduced patient dependency on opioids or barbiturates
- Reduction in the overuse of analgesic medications and risk of complications/rebound
- Reduced chance of illness due to chronic daily headache (CDH). Approximately 3% of all migraine sufferers progress to CDH. Among the predictors for this disease progression in migraine are frequency of attacks (>4 per month), obesity, and excess use of analgesic medications.

Improving the diagnosis and treatment of migraine patients in the primary care setting can improve outcomes at every level: patient and family, provider and health care system, and society at large.

Commonly Asked Questions

Why does migraine prevalence increase and decrease with changes in age?

It is not known why migraine frequency changes with age. Among male patients, the prevalence of migraine gradually increases with age, peaking around age 35. Among female patients, migraine prevalence tends to increase during the first few decades of life, peaking around 40 and then declining over the next few decades. Since these changes correspond with the female reproductive life cycle, it is reasonable to suppose that the sex steroids (such as estrogen and progesterone) are involved, but a causal relationship has not been defined. Other age-related metabolic changes may also be involved.

What are the features of migraine that make it especially challenging for providers?

Migraine is a pain condition, and with pain management, analgesic medication overuse is a risk. As pain worsens or becomes more frequent, patients tend to increase their use of analgesic medication. However, with headache patients, increasing the use of analgesics is often not a useful therapeutic strategy. Patients may incur additional costs in an attempt to achieve a pain-free state. One of the strategies to avoid analgesic medication overuse is to use migraine preventive therapies, such as beta blockers, antiepileptic drugs, or antidepressants. Although these treatments are not 100% effective in preventing migraine attacks, they may reduce the severity and frequency of attacks enough so that patients will not overuse or depend on acute medications.

Other challenges in managing migraine patients include the presence of coexisting conditions, such as depression and anxiety, and irritable bowel syndrome, as well as the cost of migraine-specific medications. If the patient also has problems such as diabetes or hypertension or other chronic medical problems, the management of these conditions may complicate the overall management of the patient and further increase the costs of care. However, appropriate management has not only been shown to improve quality of life and decrease suffering and disability, but cost-effectiveness studies have shown the financial benefit of proper treatment as well. While therapy may appear expensive, it has been found that effective treatment is cost-effective because of reduced overall medication costs (even with higher triptan costs); reduced office, ED, and urgent care visits; and fewer diagnostic tests.

BIBLIOGRAPHY

Breslau N, Lipton RB, Stewart WF, et al. *Neurology.* 2000;60: 1308-1312.

Couch JR, Stewart KE, Samuel SR, et al. Male-female differences in the migraine syndrome [abstract P04.145]. *Neurology.* 2003;60 (suppl 1):A320-A321.

Hauser WA, Annegers JF, Kurland LT. Incidence of epilepsy and unprovoked seizures in Rochester, Minnesota: 1935-1984. *Epilepsia.* 1993;34:453-468.

Hu HX, Markson LE, Lipton RB, et al. Burden of migraine in the United States: disability and economic costs. *Arch Intern Med.* 1999;159:813-818.

Lipton RB, Hamelsky SW, Kolander KB, Steiner TJ, Stewart WF. Migraine, quality of life, and depression: a population-based case-control study. *Neurology.* 2000;12:629-635.

Lipton RB, Scher AI, Kolodner K, et al. Migraine in the United States: epidemiology and patterns of health care use. *Neurology.* 2002;58:885-894.

Lipton RB, Stewart WF, Diamond S, et al. Prevalence and burden of migraine in the United States: data from the American Migraine Study II. *Headache.* 2001;41:646-657.

Lipton RB, Stewart WF, Simon D. Medical consultation for migraine: results from the American Migraine Study. *Headache.* 1998; 38:87-96.

Lipton RB, Stewart WF. Migraine in the United States: a review of epidemiology and health care use. *Neurology.* 1993;43 (suppl 3): S6-S10.

Osterhaus JT, Townsend RJ, Gandek B, Ware JE. Measuring the functional status and well-being of patients with migraine headache. *Headache.* 1994;34:337-343.

Scher AI, Stewart WF, Ricci JA, Lipton RB. Factors associated with the onset and remission of chronic daily headache in a population-based study. *Pain.* 2003;106:81-89.

Sheffield RE. Migraine prevalence: a literature review. *Headache.* 1998;38:595-601.

Sheftell FD, Tepper SJ. New paradigms in the recognition and acute treatment of migraine. *Headache.* 2002;42:58-69.

Stewart WF, Linet MS, Celantano DD, et al. Age- and sex-specific incidence rates of migraine with and without visual aura. *Am J Epidemiology.* 1991;134:1111-1120.

Stewart WF, Lipton RB, Simon D. Work-related disability: results from the American migraine study. *Cephalalgia.* 1996;16:231-238.

Vinson DR. Treatment patterns of isolated benign headache in US emergency departments. *Ann Emerg Med.* 2002;39:215-222.

Module 2
Migraine Mechanisms

Genetic Link in Migraine

Twin studies have documented the clinical observation that migraine runs in families. A strong familial influence, long apparent in migraine, has been demonstrated in twin studies. The concordance for migraine in monozygotic twins is greater than it is for dizygotic twins. However, it is also clear that the genetic background of the disorder is complex.

The molecular genetic era for migraine was heralded by the identification of 4 missense mutations in the α_{1A} subunit of the P/Q-type, voltage-gated calcium channel on chromosome 19 that is responsible for familial hemiplegic migraine (FHM) in some families. FHM is a rare subtype of migraine with aura that has a clear autosomal dominance inheritance pattern. A linkage to chromosome 19 also appears to occur in some families with more commonly occurring migraine.

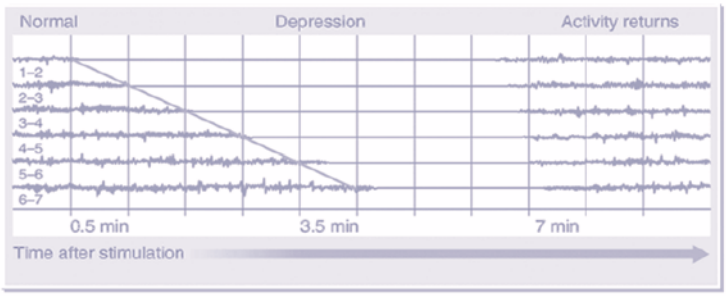
De Fusco and colleagues recently showed that the gene *ATP1A2*, which encodes the α_2 subunit of the Na+/K+ pump, is associated with familial hemiplegic migraine type 2 (FHM2) and is linked to chromosome 1q23. This mutation results in a loss of function of a single allele of *ATP1A2*. This report is the first that associates a mutation in the Na+/K+ pump to the genetics involved in migraine. Additionally, research suggests that variations within the dopamine D2 receptor gene also have some effect on susceptibility to migraine. Thus, genetic studies are providing important information about the molecular basis of migraine.

Headache Mechanisms

According to current theories on migraine with and without aura, the trigeminal vascular system serves as a common pathway for migraine pain. Although most migraine patients will never have an aura, much attention has been focused on the phenomenon. The classical, slow progression of symptoms is experienced by only 15% of patients, whereas less specific disturbances cover the whole visual field in about 25% of patients. In migraine with aura, symptoms associated with aura, such as hemianopsia, paresthesia, visual fortification, and speech difficulty, are thought to be produced by a wave of cortical neuronal spreading excitation that activates trigeminal afferent fibers on meningeal vessels and tissues and brain blood vessels. The symptoms of migrainous aura are spectacular and sometimes frightening.

Lashley calculated the rate of the characteristic slow march of symptoms to be 3–6 mm/min. This corresponds to the rate of the cortical spreading excitation that has been observed in studies of cerebral blood flow during aura. A positron emission tomography (PET) study of spontaneous migraine demonstrated a spreading, bilateral oligemia, which establishes that the phenomenon may also exist in patients with migraine without aura. It is interesting that headache starts when blood flow is still reduced, making it unlikely that vasodilatation is a cause of the pain.

Mechanism of Migraine Aura: Cortical Spreading Excitation and Depression of Leao



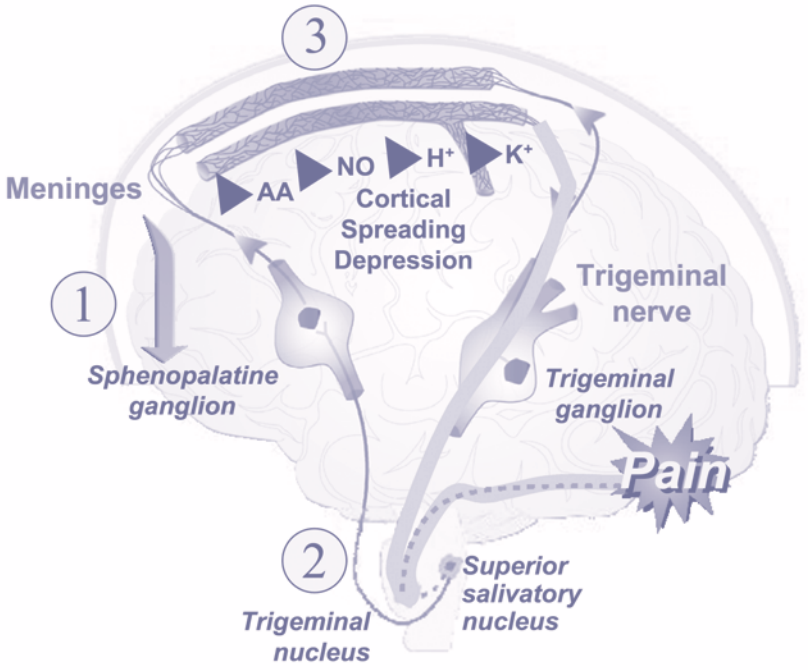
Leao AAP. *J Neurophysiol.* 1944;7:359-390; Silberstein SD et al. *Headache in Clinical Practice.* 2nd ed. London: Martin Dunitz; 2002.

The trigeminal nerve, which innervates the meninges, is intricately involved in migraine. How the migraine pain is triggered and the cascade of events following the original activation of migraine are not completely understood. Bolay and colleagues report that animal models of migraine show a connection between cortical spreading depression (CSD) and activation of trigeminal nerve afferents. Activation of the trigeminal nerve evokes a series of meningeal and brainstem events that are consistent with what is seen during a migraine attack. Specifically, triggering CSD leads to a long-lasting blood flow increase within the middle meningeal artery. This increase in blood flow depends on trigeminal and parasympathetic activation. In addition, plasma protein leakage occurs in the dura. This is the first study to specifically demonstrate that vasodilation during headache is possibly linked to a series of neurometabolic brain events, including transmission of pain via the trigeminal nerve.

In migraine with and without aura, these activated trigeminal fibers release vasoactive peptides including neurokinin A, calcitonin gene-related peptide, and substance P which promote neurogenic inflammation, protein extravasation, mast cell degranulation, and platelet activation.

Bidirectional conduction along the trigeminal nerve further sensitizes surrounding nerve fibers and conveys painful stimuli to the trigeminal nucleus caudalis in the brainstem for transmission to higher centers, producing the throbbing pain, nausea, photophobia, and phonophobia that characterize migraine.

How Does Aura Trigger Trigeminal Activation?



Adapted from Iadecola C. *Nat Med.* 2002;8:110-112. Bolay H et al. *Nat Med.* 2002;8:136-142.

Migraine and Sensitization

Patients often report increased sensory sensitivity during a migraine attack, including sensitivities to touch and temperature. With migraine, sensitization manifests as symptoms that may be regulated by central or peripheral mechanisms. Peripheral sensitization results in throbbing or that which occurs while bending over or during exercise and physical activity.

Central sensitization involves increased firing of neurons located centrally in the nucleus caudalis and may be responsible for the reported cutaneous allodynia (increased sensitivity to touch, eg, when combing hair). Not all patients report symptoms suggestive of central sensitization, but most patients will experience symptoms of peripheral sensitization such as throbbing pain and exacerbation with movement and exercise.

Many migraine patients exhibit cutaneous allodynia inside and outside their pain-referred areas during migraine attacks. Burstein and colleagues studied the development of cutaneous allodynia in migraine by measuring the pain thresholds in the head and forearms of a patient at several points during the migraine attack (1, 2, and 4 hours after onset) and compared the pain thresholds in the absence of an attack. This study demonstrated that a few minutes after the initial activation of the patient's peripheral nociceptors, these areas became sensitized and mediated the symptoms of cranial hypersensitivity. The barrage of impulses then activated second-order neurons and initiated their sensitization, mediating the development of cutaneous allodynia on the ipsilateral head. The sensitized second-order neurons activated and eventually sensitized third-order neurons, leading to allodynia on the patient's contralateral head and forearms within 2 hours, a full hour after the initial allodynia on the ipsilateral head. The authors concluded that this progression of symptoms calls for the early use of antimigraine drugs that target peripheral nociceptors before central sensitization occurs.

Migraine Without Aura: Brainstem Involvement and Suggestion of Long-Term Brain Changes in Migraine

Brainstem involvement in migraine is thought to involve the periaqueductal grey region (PAG), which has been known to be a locus in the regulation of pain pathways. Recent studies in migraine suggest that this same region is likely to be involved in regulating pain transmission in migraine. In a 2001 study by Knight and Goadsby, stimulation of the PAG in the cat inhibited evoked trigeminal neuronal activity in the animal's spinal cord. These data demonstrate that the PAG can inhibit afferent trigeminal nociceptive signals traveling to other brain centers.

Additionally, the P/Q-type channel in the PAG may be one mechanism of regulating pain signals through the brainstem. In a separate study, blockade of the P/Q-calcium channel with ω-agatoxin ICVA in the rat PAG resulted in an increase in neuronal firing of neurons on the trigeminal nucleus caudalis following activation of the dura. This study supports the role of the PAG as a modulator in descending craniovascular nociception.

In a third study, Welch and colleagues found that patients with chronic daily headache had increased iron deposition in the PAG compared with controls. Collectively, dysfunctions of the PAG may be involved in the pathophysiology of migraine in some migraine patients. Together, these studies suggest that long-term changes occur in the brain in some patients with migraine. New evidence also suggests that subclinical strokes may also occur in a subset of patients with migraine. Additional prospective and long-term studies are needed to further assess the long-term risks of migraine and treatment strategies that may reduce the risk of central nervous system changes.

BIBLIOGRAPHY

Bolay H, Reuter U, Dunn AK, Huang Z, Boas DA, Moskowitz MA. Intrinsic brain activity triggers trigeminal meningeal afferents in a migraine model. *Nat Med.* 2002;8(2):136-142.

Burstein R, Cutrer MF, Yarnitsky D. The development of cutaneous allodynia during a migraine attack: clinical evidence for the sequential recruitment of spinal and supraspinal nociceptive neurons in migraine. *Brain.* 2000;123(pt 8):1703-1709.

De Fusco M, Marconi R, Silvestri L, et al. Haploinsufficiency of ATP1A2 encoding the Na+/K+ pump alpha2 subunit associated with familial hemiplegic migraine type 2. *Nat Genet.* 2003;33(2):192-196.

Honkasalo ML, Kaprio J, Winter T, et al. Migraine and concomitant symptoms among 8167 adult twin pairs. *Headache.* 1995;35:70-78.

Iadecola C. From CSD to headache: a long and winding road. *Nat Med.* 2002;8(2):110-112.

Knight YE, Bartsch T, Kaube H, Goadsby PJ. P/Q-type calcium-channel blockade in the periaqueductal gray facilitates trigeminal nociception: a functional genetic link for migraine? *J Neurosci.* 2002;22(5):RC213.

Knight YE, Goadsby PJ. The periaqueductal grey matter modulates trigeminovascular input: a role in migraine? *Neuroscience.* 2001;106(4):793-800.

Lashley KS. Patterns of cerebral integration indicated by the scotomas of migraine. *Arch Neurol Psych.* 1941;46:331-339.

Lauritzen M. Pathophysiology of the migraine aura. The spreading depression theory. *Brain.* 1994;117(Pt 1):199-210.

May A, Ophoff, RA, Terwindt GM, et al. Familial hemiplegic migraine locus on chromosome 19p13 is involved in common forms of migraine with and without aura. *Hum Genet.* 1995;96(5):604-608.

Nyholt DR, Lea RA, Goadsby PJ, et al. Familial typical migraine: linkage to chromosome 19p13 and evidence for genetic heterogeneity. *Neurology.* 1998;50:1428-1432.

Olesen J, Friberg L, Olsen TS, et al. Timing and topography of cerebral blood flow, aura, and headache during migraine attacks. *Ann Neurol.* 1990;28(6):791-798.

Ophoff RA, Terwindt GM, Vergouwe GM, et al. Familial hemiplegic migraine and episodic ataxia type-2 are caused by mutations in the Ca2+ channel gene CACNL1A4. *Cell.*1996;87:543-552.

Peroutka SJ, Wilhoit T, Jones K. Clinical susceptibility to migraine with aura is modified by dopamine D2 receptor (DRD2) NcoI alleles. *Neurology.* 1997;49:201-206.

Welch KM, Nagesh V, Aurora SK, Gelman N. Periaqueductal gray matter dysfunction in migraine: cause or the burden of illness? *Headache.* 2001;41(7):629-637.

Wong TY, Klein R, Sharrett AR, et al, for the ARIC Investigators. Cerebral white matter lesions, retinopathy, and incident clinical stroke. *JAMA.* 2002;288:67-74.

Woods RP, Iacoboni M, Mazziotta JC. Brief report: bilateral spreading cerebral hypoperfusion during spontaneous migraine headache. *N Engl J Med.* 1994;331(25):1689-1692.

Module 3

History, Physical and Diagnosis

Patients in primary care practices have, on average, six health complaints at any given visit. Headache is among the most common symptoms encountered in primary care, and the ID Migraine™ screening criteria can help primary care professionals identify patients with headache who may require further evaluation.

The goals of this headache visit are to

- Exclude serious underlying disease as a cause for headache (secondary headache)
- Diagnose primary headache

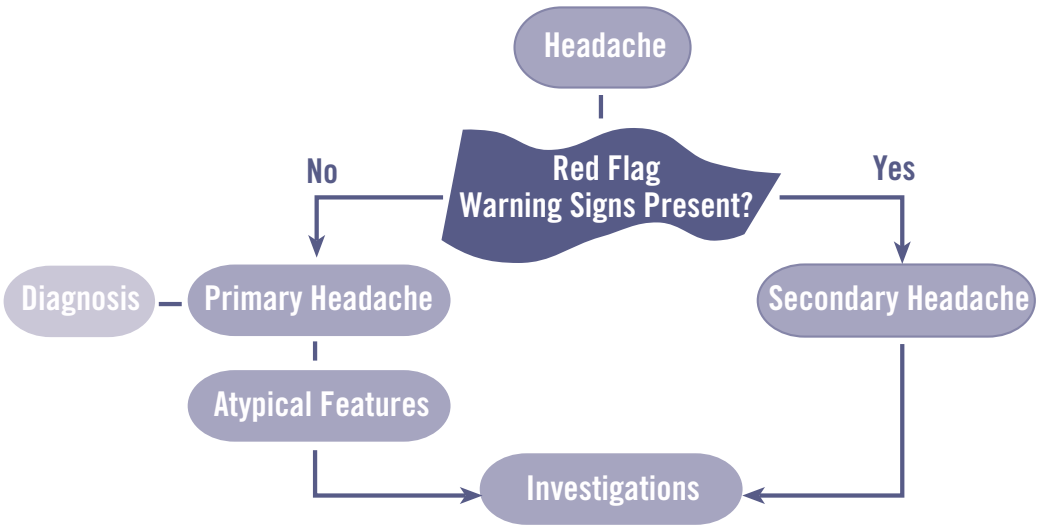
Primary Headache: A primary headache is a headache that is not a symptom of, or caused by, another disease or condition. Primary headaches fall into several common patterns, including migraine, tension-type headache (TTH), cluster headache, and chronic daily headache (CDH). Note that episodic migraine and TTH can transform to CDH, sometimes promoted by medication overuse; however, in this document, CDH is considered a primary headache. Most headache patients have primary headaches.

Secondary Headache: A secondary headache is a symptom of, or caused by, another underlying disease or condition, such as a brain tumor or infection. Secondary headaches are rare.

HEADACHE HISTORY: USEFUL QUESTIONS TO ASK PATIENTS

1. When do you think your worst headaches first started?
2. How often do you get headaches that if untreated are so severe you find it difficult to function?
3. What is the pain like and how long does it last?
4. Do you have other symptoms besides head pain with these headaches?
5. What makes your headaches better or worse?
6. How often do you take something for your headaches and what do you take?
7. Does anyone else in your family have similar headaches?
8. Do you get other kinds of headaches?
9. Has there been any recent change in your headaches?

Diagnostic Evaluation



Adapted from Silberstein SD et al. *Headache in Clinical Practice.* 2nd ed. London: Martin Dunitz; 2002.

The Modified Neurophysical Examination

This examination assumes that assessment of motor strength below the neck has been performed as part of the patient's routine physical exam and need not be repeated here. The following additional elements are recommended for the assessment of headache. Any suggestion of abnormality requires a more complete evaluation.

Examination	Comment
Pulse, blood pressure	Hypertension increases headache; uncontrolled hypertension limits treatment choices
Fundi	Increases in intracranial pressure may be cause of secondary headache
Facial muscle strength	Test function of cranial nerves—signs of secondary headache problems
Head and neck	Check range of motion and pericranial tenderness and abnormal posture
Reflexes	Suggest CNS disorder
Balance	Suggest cerebellar disorder

Swartz MH. *Textbook of Physical Diagnosis: History and Examination.* Philadelphia, PA: WB Saunders; 2002:596-628.

HISTORY AND PHYSICAL EXAMINATION

When

- Exam results are normal
- Headaches are recurrent
- Headache pattern is stable
- Headache is severe and/or temporarily disabling (impairs or prohibits activities or work, school, household responsibilities)

The likely diagnosis is **Migraine without Aura**

When

- Aura symptoms (visual symptoms, unilateral paresthesia, weakness, or speech difficulties) are also present but fully reversible

The likely diagnosis is **Migraine with Aura**

When

- Headache occurs more than 15 days per month

The likely diagnosis is **Chronic Tension-Type Headache or Chronic Migraine**

There are various challenges in diagnosing headache, including the fact that most patients have more than one type of headache, often with overlapping symptoms. Symptoms vary across and within headaches. Part of routine patient care is to assess the presence of other medical or psychiatric conditions that affect headache and watch for changes in headache patterns; individuals with migraine can develop ominous headache.

The boundaries between the headache types are indistinct. Look for patterns, and watch for changes over time. How does the headache affect the patient's life? If the headache is episodic, occurs in a stable pattern, and is severe enough to disrupt work or family life temporarily, and the physical examination is normal, the type is probably migraine. If migraines are diagnosed and successfully treated, the quality of the patient's life will be improved. Sometimes comorbid conditions such as depression or anxiety can aggravate headache conditions or have overlapping symptoms that complicate diagnosis. Thus, it is important to integrate the information gained about the headaches with information known about the patient's other health problems.

For new patients, a thorough evaluation is necessary. While migraine patients are not at higher risk for secondary causes headache (other than a small increase in risk for ischemic stroke, which can occasionally induce headache) than are nonmigraine patients, they can develop ominous causes of headache.

DIAGNOSIS: Primary Headaches

CLINICAL RULES: DIAGNOSTIC CRITERIA FOR MIGRAINE

- Attacks lasting 4–72 h (untreated or unsuccessfully treated)
- Two of the following:
  - Unilateral
  - Pulsating
  - Moderate or severe intensity
  - Aggravated by or causing avoidance of routine physical activity
- One of the following:
  - Nausea or vomiting
  - Photophobia and phonophobia
- Not attributed to another disorder

The International Headache Society (IHS) diagnostic criteria describe migraine as:

Recurrent headache disorder manifesting in attacks lasting 4 to 72 hours. Typical characteristics of the headache are unilateral location, pulsating quality, moderate or severe intensity, aggravation by routine physical activity, and association with nausea and/or photophobia or phonophobia.

Migraine is characterized by episodes of head pain that is often throbbing, frequently unilateral, and may be severe. Attacks are usually associated with nausea, vomiting, or sensitivity to light, sound, or movement. A combination of features is required for the diagnosis, but not all features are present in every attack or in every patient.

Tension-type headache is the most common form of primary headache. It is characterized by the lack of associated features. Any severe and recurrent headache is most likely to be a form of migraine and is also likely to be responsive to antimigraine therapy.

In some patients, migraine attacks are usually preceded or accompanied by neurologic symptoms that reflect transient activity in a specific area of the brain. These symptoms occur in about 15% of patients, and are usually visual; such patients have migraine with aura (previously known as classic migraine). In a recent large, population-based study, 64% of patients with migraine had only migraine without aura, 18% had only migraine with aura, and 13% had both types of migraine (the remaining 5% had aura without headache). Thus, up to 31% of patients with migraine have aura on some occasions, but clinicians who rely on the presence of aura for the diagnosis of migraine will miss many cases.

International Headache Society Diagnostic Criteria, 2004, in press.

TOP 3 DIAGNOSTIC PREDICTORS OF MIGRAINE

Because migraine is substantially underdiagnosed, a simple, 3-question, self-administered screening tool called ID Migraine™ was developed to help detect patients with unreported headache complaints in the primary care setting. The questionnaire was developed from a 9-item questionnaire that was in turn designed to evaluate patients based on the criteria for diagnosis of migraine established by the IHS. Of the 9 diagnostic screening questions, it was found that a 3-item subset of nausea, disability, and photophobia had the best performance. The sensitivity and specificity of the questionnaire were similar regardless of sex, age, presence of comorbid headaches, or previous diagnoses.

- Strongest predictors of migraine diagnosis among patients complaining of headache
  - Nausea

    Are you nauseated or sick to your stomach when you have a headache?
  - Disability

    Has a headache limited your activities for a day or more in the last 3 months?
  - Photophobia

    Does light bother you when you have a headache?

Patients complaining of headache who answer positively on 2 out of the 3 symptom questions have a 93% chance of being diagnosed with migraine by a headache expert. Those patients who answer positively on all 3 questions have a 98% chance of a migraine diagnosis.

Lipton RB, Dodick D, Sadovsky R, Kolodner K, Endicott J, Hettiarachchi J, Harrison W. A self-administered screener for migraine in primary care: the ID Migraine™ validation study. *Neurology.* 2003;61:375-382

Worrisome Headache Red Flags—"SNOOP"

Systemic **S**econdary	Symptoms such as fever or weight loss or Risk factors such as HIV or systemic cancer
Neurologic	Symptoms or abnormal signs such as confusion, impaired alertness, papilledema, asymmetry, motor weakness, nuchal rigidity, visual disturbance other than aura, dysphasia
Onset	Sudden, abrupt, split-second, seconds to minutes, rapid onset of headache
Older	New headache onset in an older patient or a progressively worsening headache in a middle-aged patient (>50 years of age)
Progression pattern	Previous headache history—A major change in attack frequency, severity, or clinical features; a first headache or different headache unlike any experienced before

USING SNOOP

Red Flags in Headache Diagnosis[1]

Headache Red Flag	Differential Diagnosis	Possible Workup
Headache with systemic illness (fever, stiff neck, rash) or New headache in a patient with HIV or cancer	Meningitis, encephalitis, Lyme disease, systemic infection, collagen vascular disease Meningitis (chronic or carcinomatous), brain abscess (including toxoplasmosis), metastasis	Neuroimaging, lumbar puncture, blood tests Neuroimaging, lumbar puncture
Neurologic symptoms or signs of disease other than typical aura	Mass lesion, arteriovenous malfunction, stroke, collagen vascular disease (including antiphospholipid antibodies), intracranial hypertension	Neuroimaging, collagen vascular evaluation
Sudden onset headache	Subarachnoid hemorrhage, pituitary apoplexy, bleed into a mass or arteriovenous malformation, mass lesion (especially posterior fossa)	Neuroimaging, lumbar puncture
Headache begins in patient >50 years of age	Temporal arteritis (giant cell arteritis), mass lesion	Erythrocyte sedimentation rate, neuroimaging
Accelerating pattern of headaches	Mass lesion, subdural hematoma, medication overuse	Neuroimaging, drug screen

[1]Adapted from Silberstein SD et al. *Headache in Clinical Practice.* 2nd ed. London: Martin Dunitz; 2002:14.

DIAGNOSIS: Secondary Headaches

- Secondary headaches, also called ominous headaches, are rare
- The lifetime prevalence of headache secondary to nonvascular intracranial disease, including tumor, is 0.5%
- A large meta-analysis determined that only 0.18% of patients with migraine symptoms and a normal neurologic exam result will have significant intracranial pathology identified through neuroimaging
- A diagnosis of migraine does not preclude the development of a secondary headache in the future. Regard a significantly changed headache as a new headache being investigated for the first time
- Abnormal findings on neurologic examination in patients with headache require further evaluation
- In a patient with no history of headaches or a patient with changed headaches that depart significantly from their normal pattern, be alert for the following things:
  - Abrupt onset of a new type of severe headache
  - Worst headache the patient has ever had
  - Progressive worsening of headache over a period of days or weeks
  - Headache precipitated by exertion such as exercise, coughing, sneezing, bending over, or sexual arousal
  - Headache accompanied by generalized illness or fever, nausea, vomiting, or stiff neck

Diagnostic Testing

Diagnostic testing rules out secondary headache. It does not diagnose primary headache.

- Laboratory testing is not routinely needed in the evaluation of headache patients
- Investigate patients with warning symptoms or signs of secondary headache
- May wish to establish baseline laboratory screen before prescribing new drugs
- Review cardiovascular risk factors prior to prescribing vasoconstricting drugs such as dihydroergotamine, or DHE, and triptans; consider electrocardiogram on a case-by-case basis
- Electroencephalogram is not useful in headache evaluation

Neuroimaging is unnecessary when

- No focal neurologic findings exist
- Patient has stable pattern of recurrent headache
- No history of seizures is present

Neuroimaging should be considered when

- Neurologic exam has abnormal findings
- Patient has progressively worsening headache
- Patient has new persistent headache
- Patient has a new, rapid onset headache (thunderclap headache)
- Headache does not respond to standard therapy

Consensus standard: magnetic resonance imaging (MRI) is more sensitive than computed tomography (CT) for most abnormalities of the central nervous system

Yield depends on

- Strength of the magnet
- Use of paramagnetic contrast
- Selection of acquisition sequences
- Use of magnetic resonance angiography and venography

Lumbar puncture is essential in patients with

- Severe, rapid onset (seconds to minutes) recurrent headache
- First or worst headache
- High or low intracranial pressure suspected
- Chronic, intractable headache that does not meet other criteria

Use lumbar puncture only after normal CT has been obtained*

Lumbar puncture should be performed if

- Neuroimaging is normal
- Neuroimaging is suggestive of a disorder that can only be diagnosed by measuring cerebrospinal fluid (CSF) pressure, cell count, and chemistries

*Neuroimaging should be performed, if possible, prior to lumbar puncture; however, if imaging is not available, lumbar puncture should be performed first if meningitis is suspected.

Ominous Causes of Headache That Routine CT May Miss

VASCULAR DISEASE

- Saccular aneurysms
- Arteriovenous malformations (especially posterior fossa)
- Subarachnoid hemorrhage
- Carotid or vertebral artery dissections
- Cerebral infarctions
- Vasculitis
- Subdural hematoma

NEOPLASTIC DISEASE

- Neoplasms (especially in the posterior fossa)
- Meningeal carcinomatosis
- Pituitary tumor and hemorrhage

CERVICOMEDULLARY LESIONS

- Chiari malformations
- Structural lesions at the foramen magnum

INFECTIONS

- Paranasal sinusitis
- Meningoencephalitis
- Cerebritis and brain abscess

DISORDERS OF INTRACRANIAL PRESSURE

- Idiopathic intracranial hypertension (pseudotumor cerebri)
- Intracranial hypotension (CSF leak)

CT can identify some, but not all, abnormalities that can cause ominous headaches. CT is usually preferable to MRI for the evaluation of subarachnoid hemorrhage in the first 24 hours, acute head trauma, and bony abnormalities.

SINUS HEADACHE IS OVERDIAGNOSED

- Sinus abnormalities other than acute purulent sinus infections are rarely the cause of headache
- Migraine is often confused with true sinus headache because these headaches have similar locations
- Headache associated with sinus disease is usually continuous, not intermittent
- Chronic sinusitis is frequently associated with facial tenderness and pain, engorged and swollen nasal mucosa, a purulent or sanguinopurulent nasal discharge, anosmia, pain upon mastication, and halitosis
- Treatment of true sinus headaches caused by allergic or microbiologic inflammation is directed at treating the underlying pathology
- Nasal and sinus-related pain can mimic primary headache syndromes, and coexistent conditions can occur

TENSION-TYPE HEADACHE (TTH)

TTH, previously called muscle tension, contraction, or stress headache, is the most common type of headache in the general population, but most sufferers do not seek medical attention. Approximately 80% of individuals with migraine also report experiencing TTH. IHS criteria for TTH include

- >10 attacks, 4 d/mo
- Pain characteristics (2 of the following)
  - Bilateral
  - Pressing/tightening (not pulsating)
  - Mild to moderate intensity
  - Not aggravated by routine activity

In addition: No nausea, vomiting, photophobia, or phonophobia (anorexia may occur)

While nausea is an important feature of migraine, sufferers do not experience nausea with every headache. Likewise, unilateral location is a prominent characteristic, although 41% of migraine sufferers report bilateral pain for at least some of their migraines. Similarly, patients with migraine report that 50% of the time the nature of their pain is not pulsating or throbbing and 30% of TTH sufferers report pulsating pain. Thus, the diagnostic overlap between migraine and TTH can make criteria for diagnosing headaches seem ambiguous when applied to the individual patient, especially if the patient suffers from more than one type of headache and experiences difficulty articulating or remembering the differences. Patients have a tendency to remember the most frequent headache or to merge the symptoms from a number of headaches into a description of a single headache. TTH can be further subdivided into episodic and chronic, the difference being that chronic TTH occurs more than 15 days per month and must be present for at least 6 months to confirm the diagnosis.

CHRONIC DAILY HEADACHE (CDH)

CDH is a term used to describe headache in patients with a group of primary headache disorders such as migraine or TTH that has evolved from episodic to chronic migraine and chronic TTH. These patients experience headache more than 15 days a month, with each headache lasting more than 4 hours a day. CDH may also occur as a result of overuse of analgesics and migraine-specific medications or may be secondary to another disease. There are a number of rare primary CDH disorders as well that are outside the scope of this program, such as hemicrania continua, new daily persistent headache, SUNCT (short-lasting unilateral neuralgiform pain with conjunctival injection and tearing), and hypnic headache. CDH can also be secondary to trauma and cervical spine disorders. Chronic migraine patients often have a history of episodic migraine beginning in their teens or twenties. Over the years, the headaches become more frequent and the associated symptoms of photophobia, phonophobia, and nausea become less severe and frequent than in typical episodic migraine. The daily headache tends to be mild to moderate with episodic full-blown migraine attacks superimposed on the less severe headaches. In population studies, less than one third of patients with these headaches overuse medications, but in clinic-based studies, about 80% of chronic migraine patients overuse medications. In some of these patients, the daily headache may be secondary to the overuse of medications. However, the presence of analgesic medication overuse does not necessarily mean cessation of overuse will lead to resolution of the daily headache.

Communicating a Migraine Diagnosis to Patients

Patients need

- A simple, clear explanation for their headaches
- Reassurance and encouragement
- Their questions answered
- Participation in decisions about their care
- A treatment plan with structured follow-up
- Realistic expectations

Time spent educating patients about their headache pays off in reduced anxiety, increased understanding of the treatment goals, and improved compliance with the treatment regimen. Patients may need reassurance that they are not mentally ill and that they do not have an undiagnosed life-threatening condition. It is important to avoid medical jargon and use language patients can readily understand.

One effective approach is to give patients examples they can understand. It can be helpful to describe their condition as involving a "sensitive brain." In this example, one or more factors such as light, stress, or hormonal changes may trigger a reaction in the brain. The result of these reactions is that chemical neurotransmitters are released that cause the sensation of pain.

Some patients may have common social biases about migraine and have difficulty accepting their diagnosis. Time spent explaining the biologic basis of migraine to them will be especially important. In the treatment phase, it is important to include the patient by explaining the treatment options and encouraging necessary lifestyle changes. Dropout from migraine treatment is high. It will be important to set realistic expectations. Like most chronic medical illnesses, migraine cannot be cured but it can be controlled, particularly if the patient becomes actively involved in management. Improvement will not come overnight.

Medication Overuse

- 80% of patients with chronic daily headache overuse their acute medications
  - Most chronic migraine patients also overuse their acute medications
- Overuse Indicators
  - Simple analgesics: >3 d/wk
  - Triptans/combination analgesics: >2 d/wk
  - Opioids/ergotamine: >2 d/wk

Triggers and Behaviors

Understanding headache triggers can help patients take control of their headaches and guide behavioral changes that may alleviate their suffering. However, trigger management will not eliminate all headaches in most patients. Too much emphasis on trigger elimination can itself diminish quality of life and contribute to the burden of disease.

Many patients have a good understanding of the factors that precipitate their migraine headaches. The response to triggers is highly individual. The list below can be used as a tool to help patients think about factors that may influence the onset of their headaches.

Guideline for Evaluating Triggers: It is a trigger if it causes headache more than 50% of the time within 24 hours.

- Triggers should not be confused with the cause of headache
- Triggers can be stress, environmental, hormonal, dietary, or behavioral (sleep)
- Not all triggers act equally to provoke headache
- There may be a "load" factor requiring the presence of multiple triggers or a combination of particular triggers to provoke headache
- Menstruation is a powerful trigger for many but not all women with migraine
- The following triggers are so common to most individuals with migraine that their general avoidance can be recommended:
  - Sleep disturbances
  - Fasting or skipping meals
  - Caffeine
  - Alcohol

Tips for a Healthy Lifestyle

- Limit caffeine consumption to less than 2 beverages per day
- Don't skip meals
- Practice good sleep hygiene
- Minimize stress

COMMON MIGRAINE TRIGGERS

Diet
Hunger
Alcohol
Additives
Certain foods

Caffeine Withdrawal

Hormonal Changes
Menstruation
Menopausal fluctuations

Environmental Factors
Light glare/visual stimuli
Odors
Altitude
Weather change

Head or Neck Pain
Trauma
Other causes

Physical Exertion
Exercise
Sex

Stress and Anxiety
Letdown

Chronobiologic
Sleep (too much or too little)
Schedule change

Caffeine

Many popular foods, beverages, and medications contain caffeine. Labeling regulations do not require caffeine content to be listed. The following list may be helpful to give patients an idea of the probable caffeine content of these and similar products they use.

CAFFEINE CONTENT OF COMMON FOODS, BEVERAGES

Product	Serving Size	Caffeine Content (mg)
Coffee		
Caffeinated	8 oz	55–130
Decaffeinated	8 oz	5
Tea		
Caffeinated	8 oz	25–100
Decaffeinated	8 oz	<5
Soft Drinks		
Colas, etc	12 oz	22.5–58
Clear sodas	12 oz	0
Frozen Desserts		
Ice creams & frozen yogurts	1 cup	8–85
Yogurts	8 oz	0–45
Chocolates or Candies	1.5–8 oz	5–72
Various		

CAFFEINE CONTENT OF MEDICATIONS

Medication	Dosage (tablets)	mg
OTC Medications		
No-Doz®, maximum strength, Vivarin®	1	200
No-Doz®, regular strength	1	100
Extra-Strength Excedrin®	2	130
Anacin®	2	64
Vanquish®	2	66
Prescription Medications		
Darvon Compound 65®	1	32.4
Fioricet®	1	40
Fiorinal® 1	1	40
Norgesic® 1	1	30
Norgesic Forte®	1	60
Synalgos-DC®	1	30

Adapted from Caffeine Content of Foods and Drugs Chart. Center for Science in the Public Interest. July 31, 1997. Available at: http://www.cspinet.org/new/cafchart.htm; and Rapoport AM, Sheftell FD. *Headache Disorders—A Management Guide for Practitioners.* Philadelphia, PA; WB Saunders: 1996:50. Martin VT, Behbehani MM. Toward a rational understanding of migraine trigger factors. *Med Clin North Am.* 2001;85;4:911-941.

Sleep

It has been theorized that individuals suffering from migraine may have a defect in chronobiologic synchronizing systems. Alterations in chronobiology, such as too little or too much sleep, can provoke migraine. Patients with migraine need to maintain proper sleep habits. The following sleep hygiene recommendations may help migraine patients regularize their sleep.

GENERAL SLEEP HYGIENE MEASURES

Wake up at the same time of day, including weekends, holidays, and vacations	Avoid heavy meals too close to bedtime, as this may interfere with sleep; a light snack may be sleep-inducing
Discontinue caffeine 4 to 6 hours before bedtime and minimize total daily use (caffeine is a stimulant and may disrupt sleep)	Regular exercise in the late afternoon may deepen sleep; vigorous exercise within 3 to 4 hours of bedtime may interfere with sleep
Avoid nicotine, especially near bedtime and upon night awakenings (nicotine is also a stimulant)	Minimize noise, light, and excessive temperature during the sleep period
Avoid use of alcohol in the late evening to facilitate sleep onset; alcohol can cause awakenings later in the night	Move the alarm clock away from the bed if it is a source of distraction

Adapted from National Institutes of Health National Center on Sleep Disorders Research and Office of Prevention, Education, and Control. Insomnia Assessment and Management in Primary Care. 1998. NIH Publication No. 98-4088. Available at: http://www.nhlbi.nih.gov/health/prof/sleep/insom_pc.pdf; and Silberstein SD, Saper JR, Freitag FG. Migraine diagnosis and treatment. In: Silberstein SD, Lipton RB, Dalessio DJ, eds. *Wolff's Headache and Other Head Pain.* 7th ed. Oxford: Oxford University Press; 2001:121-237.

Diaries

Many examples of headache diaries are available from headache-related organizations. Pharmaceutical company representatives often make them available to physicians. Some patients use them, finding them very helpful in identifying and eliminating factors that influence their headaches. Diaries can be as simple as a notebook or a wall calendar, or be quite elaborate. As a minimum, the patient should try to capture the following information:

- Date
- Time of onset and finish
- Intensity on scale of 0 to 10
- Preceding symptoms
- Suspected triggers
- Medication and dosage taken
- Relief (complete/partial/none)

A copy of a headache diary is provided on the following page. Other examples of headache diaries can be downloaded from the following Web sites:

American Headache Society/American Council for Headache Education
http://www.achenet.org/prevention/understanding/diary.php

National Headache Foundation
http://www.headaches.org/professional/educationresources/PDF/headache_diary.pdf

JAMA Migraine Information Center
http://www.ama-assn.org/special/migraine/support/educate/diary.htm

Headache Diary

The headache diary can be a useful tool to track your migraine and identify factors that influence migraine.

Month: _____ **Name:** _____

Severity Scale:

0 – Headache-free
1 – Mild headache, allowing normal activity
2 – Moderate headache, disturbing but not preventing normal activity
3 – Severe headache, normal activity is impossible. Bed rest may be necessary

Relief Measures

1. Ice pack
2. Bed rest
3. Dark room
4. Medication (list name and dosage)
5. Relaxation techniques
6. Other (please specify)

Headache Triggers

1. Alcohol
2. Chocolate
3. Aged cheese
4. Citrus fruits
5. Cured meats
6. MSG
7. NutraSweet®
8. Skipped meals
9. Nuts
10. Onions
11. Salty foods
12. Excess caffeine
13. Stress
14. Fatigue
15. Missed medication
16. Eyestrain or other visual triggers

Headache Diary (Women should circle dates of menstrual flow)

Date	Severity	Relief Measures	Headache Triggers
1			
2			
3			
4			
5			
6			
7			
8			
9			
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11			
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American Council for Headache Education, 19 Mantua Road, Mt. Royal, NJ 08061, 856-423-0258, fax 856-423-0082, achehq@talley.com.

SUMMARY

HISTORY

The goal of history and physical is to rule out secondary headache and diagnose primary headache

- Focus on the most severe headache first
- Ask standardized questions
  - Onset
  - Frequency/duration
  - Location
  - Severity
  - Characteristics and other symptoms
  - Family history
  - What makes it better/worse; medications taken
  - Any recent change in pattern
  - Other types of headaches
  - Neurologic symptoms
    - Cognitive changes
    - Changes in speech or language
    - Loss of strength/sensation (including visual loss and diplopia)
    - Vertigo and faintness
- Ask about disability: Does the headache interfere with daily life?
- Be alert for comorbid conditions complicating headache or diagnosis

PHYSICAL EXAMINATION

The goal of the physical examination is to rule out secondary or ominous headache. Abnormal signs needing further workup include

- Systemic signs
  - Abnormal blood pressure
  - Signs (or symptoms) associated with infectious disease (meningitis, acute sinusitis, brain abscess)
- Neurologic signs and symptoms
  - Papilledema (increased intracranial pressure, malignant hypertension, thrombosis of central retinal vein)
  - Motor weakness
  - Pupillary abnormalities
  - Sensory loss
  - Aphasia
  - Visual loss

DIAGNOSIS

- Assess the worst headache first
- Rule out secondary headache
- Diagnose primary headache
- When results of the modified neurologic examination are normal, episodic headache that is severe enough to interfere with the activities of daily living is most likely migraine
- Most migraine patients have more than one type of headache
- Patients who think they have stress headaches or sinus headaches probably have migraine
- If patients think they have migraine, they probably do
- TTH is usually not severe or disabling; migraine is frequently temporarily disabling
- Ask patients if they miss work or school with their headaches
- Most individuals with migraine do not have aura
- Migraine can be bilateral, occipital, or generalized
- 50% of migraine pain is not pulsating
- Sinus headache is generally a dull headache secondary to infection
- Ominous headache is rare and is almost always accompanied by neurologic or systemic signs and symptoms

DIAGNOSTIC TESTING

- Diagnostic testing rules out secondary or ominous headache; it cannot diagnose primary headache
- Diagnostic testing is useful when neurologic and systemic findings are present
- If no systemic or neurologic findings are present and the patient is experiencing typical symptoms, secondary headache is unlikely
- Engage patients in discussion of diagnostic tests to increase their understanding and help reduce overuse
- Clinical laboratory studies are generally not helpful except when acute or preventive medications will be used where an electrocardiogram and baseline chemistries could be helpful, infection is suspected, or drug level measurements are needed to assess compliance, absorption, or medication overuse
- MRI is preferred over CT except in patients with subarachnoid hemorrhage in the first 24 hours, head trauma, and bony abnormalities

TRIGGERS AND BEHAVIORS

- Triggers should not be confused with the cause of headache
- Triggers can be environmental, hormonal, dietary, or behavioral (irregular sleep, skipping meals, etc)
- Menstruation is a powerful trigger for many but not all women with migraine
- Headache diaries can be helpful tools for some patients to identify triggers

Commonly Asked Questions

HISTORY AND PHYSICAL

As a primary care physician, I feel overwhelmed by all of the conditions I am supposed to screen for. Is there a quick, efficient way to deal with a headache complaint that is on a list of multiple other problems?

Page 29 of this section includes 3 simple screening questions. It has recently been shown that patients complaining of headache who answer positively on 2 out of 3 of these questions have a 93% chance of having a diagnosis of migraine. Patients who answer 3 out of 3 of these questions positively have a 98% chance of being diagnosed with migraine. A screening question about headaches can be part of the review of systems questionnaire that many practices administer to patients. If patients identify headache as a problem on the review of systems, ask if the headaches are so bad that they miss work, social, or family activities. If so, we recommend that you arrange a separate appointment to deal with headache concerns. In the meantime, the patient can be asked to keep a headache diary and bring it to the next appointment.

I have a hard time sorting out all of the different kinds of headaches most patients describe. Is there any way to make a headache history more efficient?

Experts recommend asking the patient to begin by describing their most severe type of headache. Usually this is the headache that requires treatment. Although some patients have multiple types of headache, most of their "other" headaches are probably variations of their major headache type. Be particularly wary of patients with migraine who describe other headaches that they call "tension" or "sinus" headaches. Research has shown that most of those headaches in known migraineurs are simply a variation of migraine, and not a separate headache type.

Patients often come to me having made their own headache diagnosis. How often are they correct?

Research has established the following:

1. Patients who call their headaches migraines are usually right
2. Patients who call their headaches "stress headaches" usually have migraine
3. Patients who think they have sinus headaches, in the absence of corroborating signs or symptoms such as fever or purulent nasal discharge, usually have migraine

What's the most highly "overrated" symptom of migraine?

Aura. Only 15% of migraine patients experience aura.

DIAGNOSIS

Why is migraine frequently misdiagnosed as sinus headache?

Migraine is often accompanied by sinus/allergy-like symptoms such as stuffy and runny nose and feelings or pain or pressure in or around the sinuses, which patients and physicians alike may misinterpret as sinus headache. Migraine sufferers also describe attacks that are precipitated by changes in weather or during bouts of allergic rhinitis. Appropriate diagnosis allows avoidance of unnecessary and possibly harmful antibiotic therapy or surgery for presumed "sinus" problems.

How can I tell the difference between migraine and a severe TTH?

There is no such thing as a severe tension-type headache. By definition, TTH is mild or moderate in intensity. Severe headaches are likely to be migraine, especially if they are accompanied by nausea and temporary disability, and aggravated by physical activity. Gastrointestinal (GI) symptoms are uncommon in TTH and very common in migraine. Although TTH can be bothersome, especially if frequent, they usually do not require the sufferer to suspend or significantly curtail activity. TTH is not aggravated by routine activity such as climbing stairs or bending over to pick things up, while migraine frequently is.

Other than abnormal neurologic examination findings, are there any other "tip offs" that you may be dealing with an ominous headache?

Be alert for patients who complain of a single, persistent headache, irrespective of severity, especially when there is no previous history of episodic headaches. Similarly, closer scrutiny is warranted for patients who tell you their current headache is a new headache unlike any previous pattern of headache (see SNOOP criteria for secondary headache, page 30).

Are some migraine patients more likely than others to be misdiagnosed?

One of our case patients, Peter, is a good example of a migraine patient at risk of receiving an incorrect diagnosis. He is a white male over age 40 and thus does not fit the stereotype that all migraine sufferers are young women. Peter also has an entrenched belief that he suffers from sinus headache and is likely to self-treat until his headaches become unmanageable.

Some patients have a pattern of mild, continuous headache that seems like TTH, but also have superimposed episodes of severe headache that are clearly migraine. What is the diagnosis in this situation?

This headache pattern is termed "chronic migraine." In most patients, it evolves over time from an initial pattern of episodic migraine. Medication overuse is suspected of being an important (but not the only) cause of this transformation. Chronic migraine is a diagnostic challenge because of the overlapping symptoms of chronic TTH and superimposed migraine. It is useful to ask what the patient's initial headache pattern was like. Most often you will hear a classic history of episodic migraine that, over the years, became more and more frequent, with the eventual development of a constant, low level of pain and superimposed characteristic migraine attacks.

DIAGNOSTIC TESTING

Is laboratory testing ever useful in headache diagnosis?

Laboratory testing can be useful to rule out specific suspected causes of secondary headache or can establish baseline conditions prior to prescribing therapy, and can monitor drug levels.

What is a thunderclap headache?

Thunderclap headache is the sudden onset of a severe headache that reaches peak intensity in less than 1 minute. Thunderclap headache should always prompt neuroimaging. It is usually benign but may indicate subarachnoid hemorrhage or venous sinus thrombosis (these disorders should be highlighted as physicians will be prompted to consider imaging the arterial and venous systems during an MRI scan).

Should an electrocardiogram always be performed before prescribing a triptan?

Most patients with migraine are young, healthy women with few or no cardiovascular risk factors. Expert consensus is that triptan prescription in these patients does not require cardiac evaluation. Some physicians prefer to obtain an electrocardiogram on all patients over age 40, while others believe this is unnecessary in the absence of specific risk factors. Patients with known coronary artery disease (CAD) should not be prescribed triptans. Clinicians may wish to evaluate the presence of coronary artery calcium deposits by ordering an electron beam CT (EBCT) to help exclude patients with CAD. If you are contemplating CAD screening based on CAD risk factors, this screening should be done regardless of considering prescribing triptans.

Why is MRI preferred over CT and in what circumstances would CT be preferable?

MRI is generally considered superior for detecting vascular disease, neoplastic disease, cervicomedullary lesions, and infections. CT is preferred for the detection of subarachnoid hemorrhage within the first 24 hours.

BIBLIOGRAPHY

Blumenthal HJ. Headaches and sinus disease. *Headache.* 2001; 41:883-888.

Buring JE, Hebert P, Romero J, et al. Migraine and subsequent risk of stroke in the Physicians' Health Study. *Arch Neurol.* 1995;52: 129-134.

Cady RK, Schreiber CP. Sinus headache or migraine. *Neurology.* 2002;58(suppl 6):S10-S14.

Cady RK, Schreiber CP, Billings C. Subjects with self-described "sinus" headache meet IHS diagnostic criteria for migraine. *Cephalalgia.* 2001;21:298.

Center for Science in the Public Interest. Caffeine Content of Foods and Drugs. July 31, 1997. Available at: http://www.cspinet.org/new/cafchart.htm. Accessed February 3, 2003.

Central Brain Tumor Registry of the US. Primary brain tumors: incidence by gender, race, and age. Statistical Table 7. Available at: http://www.cbtrus.org/2001/table2001_7.htm. Accessed January 30, 2003.

Diamond ML. The role of concomitant headache types and non-headache co-morbidities in the underdiagnosis of migraine. *Neurology.* 2002;58(9 suppl 6):S3-S9.

Evans RW, Rozen TD, Adelman JU. Neuroimaging and other diagnostic testing in headache. In: Silberstein SD, Lipton RB, Dalessio DJ, eds. *Wolff's Headache and Other Head Pain.* 7th ed. Oxford: Oxford University Press; 2001:247-282.

Kaniecki RG. Diagnostic challenges in headache – migraine as the wolf disguised in sheep's clothing. *Neurology.* 2002;58(9 suppl 6): S1-S2.

Lipton RB, Stewart WF, Diamond S, et al. Prevalence and burden of migraine in the United States: data from the American Migraine Study II. *Headache.* 2001;41:646-657.

Lipton RB, Stewart WF, Liberman JN. Self-awareness of migraine: interpreting the labels that headache sufferers apply to their headaches. *Neurology.* 2002;58(9 suppl 6):S21-S26.

Martin VT, Behbehani MM. Toward a rational understanding of migraine trigger factors. *Med Clin North Am.* 2001;85;911-941.

Mattson P, Svardsudd K, Lundberg PO, Westerberg CE. The prevalence of migraine in women aged 40-74 years: a population-based study. *Cephalalgia.* 2000;20;10:893-899.

Newman LC, Solomon S. Infectious, toxic, and metabolic headache. In: Silberstein SD, Lipton RB, Dalessio DJ, eds. *Wolff's Headache and Other Head Pain.* 7th ed. Oxford: Oxford University Press; 2001: 434-446.

Olesen J (corresponding author). Classification and diagnostic criteria for headache disorders, cranial neuralgias and facial pain. Headache Classification Committee of the International Headache Society. *Cephalalgia.* 1988;8(suppl 7):1-96.

Pryse-Phillips WEM, Dodick DW, Edmeads JG, et al. Guidelines for the diagnosis and management of migraine in clinical practice. *Can Med Assoc J.* 1997;156;9:1273-1287.

Rapoport AM, Sheftell FD. *Headache Disorders–A Management Guide for Practitioners.* Philadelphia, PA; WB Saunders: 1996: 100-104.

Rasmussen BK, Jensen R, Schroll M, Olesen J. Epidemiology of headache in a general population – a prevalence study. *J Clin Epidemiol.* 1991;44:1147-1157.

Report of the Quality Standards Subcommittee of the American Academy of Neurology. Practice parameter: the utility of neuroimaging in the evaluation of headache in patients with normal neurological examinations [summary statement]. *Neurology.* 1994;44:1353-1354.

Russell MB, Rasmussen BK, Fenger K, Olesen J. Migraine without aura and migraine with aura are distinct clinical entities: a study of four hundred and eighty-four male and female migraineurs from the general population. *Cephalalgia.* 1996;16;4:239-245.

Schor DI. Headache and facial pain – the role of the paranasal sinuses: a literature review. *Cranio.* 1993;11;1:36-47.

Silberstein SD, Lipton RB, Goadsby PJ, Smith RT. *Headache in Primary Care*. Oxford, England: Isis Medical Media Ltd; 1999:1-5.

Silberstein SD, Lipton RB, Goadsby PJ. *Headache in Clinical Practice*. 2nd ed. London, England: Martin Dunitz; 2002:31-40.

Silberstein SD, Lipton RB. Chronic daily headache. In: Silberstein SD, Lipton RB, Dalessio DJ, eds. *Wolff's Headache and Other Head Pain.* 7th ed. Oxford: Oxford University Press; 2001:247-282.

Sheftell FD, Tepper SJ. New paradigms in the recognition and acute treatment of migraine. *Headache.* 2002;42:58-69.

Stewart WF, Linet MS, Celantano DD, et al. Age- and sex-specific incidence rates of migraine with and without aura. *Am J Epidemiology.* 1991;134:1111-1120.

Swartz, MH. *Textbook of Physical Diagnosis: History and Examination*. Philadelphia, PA: WB Saunders; 2002:596-628.

Wall M, Silberstein SD, Aiken RD. Headache associated with abnormalities in intracranial structure or function: high cerebrospinal fluid pressure headache and brain tumor. In: Silberstein SD, Lipton RB, Dalessio DJ, eds. *Wolff's Headache and Other Head Pain.* 7th ed. Oxford: Oxford University Press; 2001:393-416.

Module 4

Migraine Management

This section provides an overview of treatment approaches for migraine. Many patients are undertreated, which is indicated by the low use of migraine-specific medications, reported ongoing disability, and overall treatment dissatisfaction. Screening for migraine routinely in primary care offices will help identify those patients who may be headache or migraine sufferers and who may benefit from a more aggressive treatment management plan. Education about lifestyle issues and aggravating factors are important. Appropriate use of acute and preventive migraine treatments will also improve overall treatment efficacy rates and patient satisfaction with therapy.

Nonpharmacologic approaches are often dismissed as not useful or too time-consuming. However, simple behavior changes can play a critical role in achieving control of a deteriorating or disabling headache condition. This includes addressing stress levels and issues such as sleep, diet, over-the-counter medications, and caffeine. Migraine is optimally managed like any other chronic illness such as diabetes, hypertension, and asthma. Successful treatment depends on the patient committing to their own well-being and following the treatment plan specifically designed and managed by their health care provider.

STRATEGIES FOR MIGRAINE TREATMENT

Treatment can be acute, preemptive, or preventive.

Acute treatment is initiated during an attack to relieve pain and disability and to stop progression of the attack.

Preemptive treatment is used when a known headache trigger exists, such as exercise or sexual activity, and for patients experiencing a time-limited exposure to a trigger, such as ascent to a high altitude or menstruation.

Preventive treatment is maintained for months or even years to reduce attack frequency, severity, and duration. Patients taking preventive medication can also use acute and preemptive medication.

CUSTOMIZING TREATMENT

Patients with migraine should be assessed for multiple factors including attack frequency, attack variability, migraine-induced disability, and overall treatment outcomes. Baseline measures need to be established so long-term treatment outcomes can be evaluated. It is important to recognize if patients have more than one type of headache and different types/severity of attacks. Being able to identify which attacks may become more severe will help patients determine treatment choice. This will help assess if treatment is working or not working, or if there are other factors that are exacerbating headache, such as comorbid depression, other medications, or life issues such as stress and diet. Evaluating treatment response is also important in order to customize a treatment plan for patients. Prior success or failures with different formulations, time to treatment, and medication choice will help maintain an effective treatment plan over time.

ACUTE TREATMENT

ACUTE TREATMENT GOALS

- Treat attacks quickly and consistently and avoid recurrence
- Restore patient function in personal, social, and work domains
- Minimize the use of backup and rescue medications
- Eliminate or minimize adverse events (AEs)
- Optimize self-care and reduce subsequent need for resource use
- Provide cost-effective care

When planning treatment, the following factors must be considered:

- Patient's age
- Current health status (eg, migraine-specific agents may not be used in patients with compromised cardiovascular systems)
- Coexistent illnesses (eg, if planning a preventive medication, comorbidity can be leveraged to maximize therapy)
- Migraine type (eg, patients with chronic migraine will require close monitoring of medication consumption)

Select medication on the basis of the following to increase likelihood of treatment success:

- Frequency
- Severity
- Disability (eg, as disability increases, nonspecific treatments are less likely to work)
- Associated symptoms such as nausea
- Previous response to therapy

When selecting a migraine-specific agent, consider

- How quickly the headache builds
- Duration
- Tendency for recurrences
- AEs
- Patient preference

Nearly all patients will need acute medications. Patients should be offered an appropriate backup medication should their acute medication fail to provide relief. The backup can be a second dose of the acute medication or a follow-up dose of a different class of drug. For example, if the initial treatment was an oral triptan, the backup could be an injectable or oral nonsteroidal antiinflammatory drug (NSAID) or a second dose of a triptan.

In the event of complete treatment failure, patients should have a rescue medication to use at home. The rescue medication may not eliminate the pain entirely, but it should provide sufficient relief to prevent a visit to the emergency department. Rescue drugs can be potent opioids, narcotics, antiemetics, or neuroleptics.

When offering samples to patients, it is important to provide only one brand in a class of a drug at a time to make sure that the drug gets an uninterrupted trial. This will help assess medication efficacy before switching to another drug.

PRINCIPLES OF ACUTE TREATMENT

- Enlist the patient in a therapeutic alliance
- Treat the headache as early in the attack as possible to reduce the intensity and duration of the attack and minimize the associated symptoms
- Tailor treatment to both the individual and the specific attack. Headaches vary across individuals and attacks
- Limit acute medication use to two to three times per week
- Monitor medication use
- Use the correct dose. Some drugs come in more than one dose but have a dose that has been demonstrated to be optimal for most patients in clinical trials
- Give drugs a full therapeutic trial at the correct dose before switching to another drug
- Match the formulation to the symptom profile. If the patient has significant nausea, nonoral routes of administration will be preferred. If recurrence is a problem, select a medication with a superior profile on this measure
- Everyone benefits from behavioral strategies to minimize headache frequency and impact
- Consider the addition of preventive therapy for selected patients
- Provide acute therapy to treat breakthrough headaches for patients receiving preventive therapy

TYPES OF ACUTE MEDICATIONS

Drug	Dose/Frequency	Rebound Headache Potential	Remarks
ANALGESICS/COMBINATION ANALGESICS FOR MILD TO MODERATE MIGRAINE			
Aspirin (Bayer®, Bufferin®, etc) 325/500 mg Oral	Max initial dose: 1 g; can repeat q6h; max daily dose: 4 g	Yes	Limit use to no more than 2 d/wk; should not be used in patients with renal and GI diseases
Acetaminophen (Tylenol®, Datril®, etc) 325/500 mg Oral	Max initial dose: 1 g; can repeat q6h; max daily dose: 4 g	Yes	Limit use to no more than 2 d/wk; should not be used in patients with renal and GI diseases
Diclofenac K (Cataflam®) 25/50/75 mg Oral	Initial dose is 50 mg, followed by 25–50 mg after 2 h; max daily dose: 150 mg	Unlikely	Use lowest effective dose; should not be used in patients with renal and GI diseases
Flurbiprofen (Ansaid®) 50/100 mg Oral	Initial dose is 50 or 100 mg; max daily dose: 300 mg	Unlikely	Use lowest effective dose; should not be used in patients with renal and GI diseases

Drug	Dose/Frequency	Rebound Headache Potential	Remarks
Ibuprofen (Advil®, Motrin®, Nuprin®, etc) 200/300/400/600/800 mg Oral	Max initial dose: 800 mg; can repeat q6h	Unlikely	Use lowest effective dose; avoid doses >2.4 g/d; should not be used in patients with renal and GI diseases
Naproxen sodium (Aleve®, Anaprox®) Naproxen (Naprosyn®) 220/275/550 mg Oral	Max initial dose: 825 mg; can repeat q6h	Unlikely	Use lowest effective dose; avoid doses >1.5 g/d; naproxen sodium is absorbed more rapidly than naproxen
Ketorolac (Toradol®) 15 mg/mL IM/IV 30 mg/mL IM/IV 60 mg/mL IM/IV 10 mg tablets	Multiple-dose therapy: 30 mg IM or IV q6h; max daily dose: 120 mg; single-dose therapy: 60 mg IM or 30 mg IV	Unlikely as prescribed	Not for daily use; do not use for more than 5 consecutive days; drowsiness and nausea common AEs. Should not be used in patients with renal and GI diseases; tablets should be used only as continuation therapy to injection. Lower doses should be used in patients >65 years old or <50 lb
Piroxicam SL (Feldene®) 10/20 mg Oral	20 mg once daily; may be given in divided dose	Unlikely	Limit use to no more than 2 d/wk; should not be used in patients with renal and GI diseases
Aspirin/Acetaminophen + caffeine combination (Excedrin®) 250 mg Oral	Max initial dose: 500 mg; can repeat q6h; max daily dose: 4 g	Yes	Limit use to no more than 2 d/wk
Isometheptene mucate 65 mg, dichloralphenazone 100 mg, acetaminophen 325 mg (Midrin®, Isopap®, Isocom®) Oral	Max initial dose: 2 capsules at onset; can repeat 1 capsule every h if needed; max daily dose: 5/12 h, 20/mo	Yes	Limit use to no more than 2 d/wk; drowsiness, dizziness, nausea
Butalbital 50 mg, aspirin 325 mg, caffeine 40 mg (Fiorinal®) Oral	Max initial dose: 2 tablets at onset; can repeat 1 tablet q4–6h if needed; max daily dose: 5 tablets/d, 15/mo	Yes	Limit use to no more than 2 d/wk
Butalbital 50 mg, acetaminophen 325 mg, caffeine 40 mg (Fioricet®, Esgic®) Oral	Max initial dose: 2 tablets at onset; can repeat 1 tablet q4–6h if needed; max daily dose: 5 tablets/d, 15/mo	Yes	Limit use to no more than 2 d/wk

Drug	Dose/Frequency	Rebound Headache Potential	Remarks
MIGRAINE-SPECIFIC AGENTS FOR MODERATE TO SEVERE MIGRAINE			
Sumatriptan (Imitrex®)* 6 mg SC	Max initial dose: one 6-mg injection at onset; can repeat in 1 h if needed; max daily dose: 12 mg	Yes	Associated with a very rapid onset of action; especially useful when nonoral route of administration is needed
Sumatriptan (Imitrex®)* 25/50/100 mg Oral	Maximum initial dose 100 mg; can repeat q2h; max daily dose: 200 mg	Yes	Three tablet strengths provide dosing options for patients
Sumatriptan (Imitrex®)* 5/20 mg Transnasal	5, 10, or 20 mg; if headache recurs, dose can be repeated once after 2 h; max daily dose: 40 mg	Yes	Associated with a very rapid onset of action; especially useful when nonoral route of administration is needed; dose above 20 mg does not provide greater relief than 20-mg dose
Zolmitriptan (Zomig®)* 2.5/5 mg Oral	Recommended initial dose is 2.5 mg; can repeat in 2 h; max daily dose: 10 mg	Yes	Higher potency than sumatriptan allows lower doses of zolmitriptan
Zolmitriptan® (Zomig-ZMT™)* 2.5/5 mg Orally disintegrating tablet	Recommended initial dose is 2.5 mg; can repeat in 2 h; max daily dose: 10 mg	Yes	Especially useful when nausea is present and a discreet route of administration is needed or patient has difficulty swallowing tablets
Zolmitriptan (Zomig® Nasal Spray)* 5 mg Intranasal	Recommended initial dose is 5 mg; can repeat in 2 h; max daily dose: 10 mg	Yes	Associated with a very rapid onset of action; especially useful when nonoral route of administration is needed
Rizatriptan (Maxalt®)* 5/10 mg Oral	Recommended initial dose is 10 mg; can repeat in 2 h; max daily dose: 30 mg	Yes	10-mg dose has shown higher efficacy for most patients in clinical trials
Rizatriptan (Maxalt MLT®)* 5/10 mg; contains phenylalanine Orally disintegrating tablet	Recommended initial dose is 10 mg; can repeat in 2 h; max daily dose: 30 mg	Yes	Especially useful when nausea is present and a discreet route of administration is needed or patient has difficulty swallowing tablets

Drug	Dose/Frequency	Rebound Headache Potential	Remarks
Naratriptan (Amerge®)* 1/2.5 mg Oral	Recommended initial dose is 1 or 2.5 mg; can repeat once after 4 h; max daily dose: 5 mg	Yes	Associated with a slower onset of action and lower recurrence rate
Almotriptan (Axert™)* 6.25/12.5 mg Oral	Either 6.25 or 12.5 mg initial dose is recommended on an individual basis; can repeat once after 2 h; max daily dose: 25 mg	Yes	Reduced dosages are recommended in patients with severe renal disease or hepatic impairment
Frovatriptan (Frova™)* 2.5 mg Oral	Recommended initial dose is 2.5 mg; can repeat once after 2 h; max daily dose: 7.5 mg	Yes	
Eletriptan (Relpax®)* 20/40 mg Oral	Recommended initial dose is 40 mg; can repeat once after 2 h; max daily dose: 80 mg	Yes	Not to be used if the following medicines have been used within the last 72 hours: ketoconazole (Nizoral®), itraconazole (Sporonox®), nefazodone (Serzone®), troleandomycin (TAO), clarithromycin (Biaxin®), ritonavir (Norvir®), and nelfinavir (Viracept®)
Dihydroergotamine – DHE (Migranal®)** 4 mg/mL (0.5 mg) contains caffeine Intranasal Spray	Recommended initial dose: 1 spray in each nostril, repeat 15 min later. Max daily dose: 8 sprays; and 24 sprays/wk	No	Pretreatment with an antiemetic may be needed; can use perimenstrually for menstrual migraine
Dihydroergotamine – (DHE-45®)** 0.5–01 mg IM/IV/SC	Initial recommended dose of 1 mL IV, IM, or SC; can be repeated, as needed, at 1-h intervals to a total dose of 3 mL for IM or SC delivery or 2 mL for IV delivery in a 24-h period. The total weekly dosage should not exceed 6 mL	No	Pretreatment with an antiemetic may be needed; can use perimenstrually for menstrual migraine
Ergotamine tartrate (Ercatab®)** Ergotamine tartrate 1 mg, caffeine 100 mg Oral	Max initial dose: 2 tablets at onset of attack; can repeat 1 tablet every ½ hour if needed to a max of 6 tablets/attack, 10 tablets/wk	Yes	Use subnauseating dose; pretreatment with an antiemetic may be needed; can use perimenstrually for menstrual migraine

Drug	Dose/Frequency	Rebound Headache Potential	Remarks
Ergotamine tartrate (Cafergot®)** Ergotamine tartrate 2 mg, caffeine 100 mg Rectal	Max initial dose: 1 suppository at onset; can repeat in 1 h; max 2/d, 12/mo	Yes	Use subnauseating dose; pretreatment with an antiemetic may be needed; limit use to no more than 2 d/wk; can use perimenstrually for menstrual migraine; do not give with other vasoconstrictors, sympathomimetics, macrolides, propranolol, nicotine
ANTIEMETICS			
Chlorpromazine IM 0.1–1 mg/kg IV 12.5–37.5 mg	Can be administered as rapid drip diluted in 20–30 mL of saline or "slow push"	No	Adjunct therapy. Caution: possible dystonic reaction, postural hypotension, and sedation may occur
Metoclopramide Oral 10 mg Rectal 20 mg IM 10 mg IV 5 mg/mL	1 dose 30 min before taking acute drug when nausea is present. IV dosage: 0.1 mg/kg–10 mg	No	Adjunct therapy. Caution: possible dystonic reaction and sedation may occur. Metoclopramide IV may be used as a monotherapy for migraine pain; IM formulation is not effective as monotherapy, but may be used as an add-on therapy to other drugs to aid absorption
Prochlorperazine (Compazine®) Tablets 5/10 mg Capsules 10/15 mg Rectal 2.5/5/25 mg IM 5–10 mg IV 2.5–10 mg	Can be administered as a suppository, IV saline drip, or "slow push"		Adjunct therapy. Caution: possible dystonic reaction, drowsiness, or sedation may occur
CORTICOSTEROIDS			
Dexamethasone (Decadron®) .5/.75/4 mg tablets	1.5 mg BID for 2 d with a taper over 3 more d	No	Adjunct rescue therapy. Used to treat status migrainosus. Dexamethasone phosphate available as injection and other formulations
Methylprednisolone sodium succinate (Solu-Medrol®) Plus antiemetics	100 mg via saline drip over 10 min q6h for 24 h; q8h for 24 h; q12h for 24 h; and then a final dose	No	Adjunct rescue therapy. Used to treat status migrainosus

Drug	Dose/Frequency	Rebound Headache Potential	Remarks
OPIOIDS FOR MODERATE TO SEVERE MIGRAINE IN PATIENTS WHO CANNOT TAKE MIGRAINE-SPECIFIC AGENTS AND RECEIVE INADEQUATE RELIEF FROM OTHER CLASSES OF DRUGS			
Acetaminophen with codeine*** 300/15 mg 300/30 mg 300/60 mg	Single-dose range 300/15–1000/60 mg Max daily dose: 4000/360 mg	Yes	Lightheadedness, dizziness, sedation, nausea and vomiting, shortness of breath; caution: beware of dependence
Butorphanol*** (Stadol NS®) 10 mg/mL in a 2.5 mL bottle Nasal Spray IM 1–4 mg IV 1 mg 1 mg/mL, 2 mg/mL	Nasal spray: initially 1 spray (1 mg) in 1 nostril, repeat after 60–90 min if needed; or, may give 1 spray in each nostril, may repeat after 3–4 h as needed	Yes	Rapid onset of action; can cause dizziness, drowsiness, nausea, euphoria; dependency potential; use as rescue therapy; limit use due to risk of rebound and medication overuse
Hydromorphone*** (Dilaudid®) 8 mg Oral	Usual initial dose is 2–4 mg q4–6h; evaluate clinical situation	Yes	Sedation, nausea, and dizziness; caution: beware of dependency
Meperidine*** (Demerol®) IM	Usual dose is 50–150 mg q3–4h	Yes	Lightheadedness, dizziness, sedation, nausea, vomiting, and sweating; oral formulation is inconsistently and poorly absorbed; caution: beware of dependency
Morphine*** 30–60 mg Oral	Initial dose: 60 mg; may repeat with 30 mg; q3–4h	Yes	Rapid onset of action. Respiratory depression, decreased cough reflex, nausea, vomiting, constipation, itching, sedation, confusion, miosis, and hypotension (hypovolemic or orthostatic)
Nalbuphine*** (Nubain®) IM/IV/SC 10–20 mg	Usual dose is 10 mg; max dose is 20 mg; may repeat q3–6h; max daily dose: 160 mg	Yes	Sedation, nausea, and vomiting; lower drug abuse potential than codeine and propoxyphene
Oxycodone*** (Percocet®/Percodan®) Oxycodone 5/7.5/10 mg Acetaminophen 325/500/650 mg Oxycodone HCl 4.5 mg Oxycodone terephthalate 0.38 mg Aspirin 325 mg	Usual dose 1 tablet q6h	Yes	Lightheadedness, dizziness, sedation, nausea, and vomiting; caution: beware of dependency

Drug	Dose/Frequency	Rebound Headache Potential	Remarks
Propoxyphene-N*** (Darvocet®/Darvon®) propoxyphene HCl 32/65/100 mg propoxyphene napsylate 50/100 mg acetaminophen 325/500/650 mg	Initial dose is usually 1 tablet; may repeat q4h if needed; max daily dose: 6 tablets	Yes	Dizziness, sedation, nausea and vomiting; caution: beware of dependency

*Triptans: Limit use to no more than 2 d/wk; not to be used if ergotamine derivatives, triptans, or methysergide have been used in prior 24 h; screen for asymptomatic cardiac disease in patients at risk. Contraindicated in patients with risk of heart disease, basilar or hemiplegic migraine, or uncontrolled hypertension. Based on post-marketing information, rare incidences of myocardial infarction and stroke have been reported. Common AEs for the triptans include transient feelings of pain or tightness in the chest or throat, tingling, heat, flushing, heaviness or pressure, drowsiness, fatigue, or malaise.

**Ergotamine derivatives/DHE: Limit use to no more than 2 d/wk; not to be used if ergotamine derivative or other triptans have been used in prior 24 h; screen for asymptomatic cardiac disease in patients at risk. Potentiated by protease inhibitors, macrolides, azole antifungals, saquinavir (Invirase®), nefazodone (Serzone®), fluoxetine (Prozac®), fluvoxamine (Luvox®), zileuton, (Zyflo®), propranolol (Inderal®), grapefruit juice, nicotine. Contraindicated in patients with risk of heart disease, basilar or hemiplegic migraine, or uncontrolled hypertension. Contraindicated with concomitant ritonavir (Norvir®), nelfinavir (Viracept®), indinavir (Crixivan®), erythromycin, clarithromycin (Biaxin®), troleandomycin (TAO), ketoconazole (Nizoral®), itraconazole (Sporonox®), or other vasoconstrictors.

***Opioids: Monitor opioid usage carefully; do not issue phone refills; impose strict daily and weekly limits.

Adapted from: Davidoff RA. *Migraine: Manifestation, Pathogenesis, and Management.* Philadelphia, PA: FA Davis; 1995.

Ramadan NM, Silberstein, SD, Freitag FG. Evidence-based guidelines for migraine headache in the primary care setting: pharmacological management for prevention of migraine. April 25, 2000. Available at: http://www.aan.com/professionals/practice/pdfs/gl0090.pdf. Accessed October 22, 2003.

Silberstein SD, Saper JR, Freitag FG. Migraine diagnosis and treatment. In: Silberstein SD, Lipton RB, Dalessio DJ, eds. *Wolff's Headache and Other Head Pain.* 7th ed. Oxford: Oxford University Press; 2001:121-237.

Physicians' Desk Reference®. Montvale, NJ: Medical Economics Company; 2003.

SPECIFIC HEADACHE POPULATIONS

MENSTRUAL MIGRAINE

Menstrually related migraine can occur prior to, during, or after menstruation. It can also occur at the time of ovulation. Determining the actual prevalence of menstrual migraine in the population is difficult because the definitions vary.

Treatment considerations for menstrual migraine include

- Triptans given acutely are effective
- Short-term, effective prophylactic premenstrual treatment includes
  - NSAIDs in adequate dose 1 to 2 days before the expected onset of headache and continued for the duration of vulnerability. If the first NSAID fails, try a different NSAID from another chemical class
  - Scheduled doses of triptans, started 2 to 3 days before the expected headache onset and continued for a total of 5 days, also seem helpful
  - Ergotamine tartrate at bedtime or twice a day can be used at the time of menses
  - Dihydroergotamine nasal spray given every 8 hours for 6 days beginning 3 days before the expected onset of headache can also be effective
- Patients with intractable menstrual migraine may benefit from continuous use of an oral contraceptive (OC), with breaks every 3 to 4 months. The use of OCs in women with migraine with aura is controversial because of a slightly increased risk of stroke. For most women who have migraine without aura, the benefits of reliable, effective contraception outweigh the dangers of OC use. OC use in women who have migraine with aura should be assessed on a case-by-case basis
- For all migraine patients, if OCs are begun, use the lowest possible estrogen dose and monitor for worsening headache or neurologic accompaniments

Determining when the patient gets her menstrually related migraine has implications for treatment because premenstrual migraine may be related to premenstrual syndrome (PMS), while migraine during menstruation is associated with dysmenorrhea. Medications that are useful in treating headache related to dysmenorrhea may not be helpful in treating migraine associated with PMS. Diuretics and vitamins are commonly used but are ineffective treatments for menstrual migraine.

MIGRAINE IN CHILDREN

- Migraine may be different in children
  - Fast onset and resolution
  - Often relieved with sleep
- Proven efficacy of nonspecific treatments
  - Acetaminophen 15 mg/kg/dose
  - Ibuprofen 7.5–10 mg/kg/dose
- Triptans
  - Evidence lacking (short duration of attacks)
  - Expert opinion: effective and well tolerated

To date, several studies have been done that evaluate the efficacy of nonspecific migraine medications in children. Specifically, Hamalainen and colleagues (1997) evaluated ibuprofen 7.5 to 10 mg/kg/dose vs placebo in 88 children aged 4 to 15 years. Lewis and Qureshi (2000) evaluated ibuprofen vs placebo (84 children aged 6 to 12 years [ibuprofen, n=45; placebo, n=39]) for the acute treatment of migraine. Ibuprofen was associated with a 76% responder rate vs 53% for placebo (P=0.006). Several studies have also evaluated the efficacy of triptans (sumatriptan, rizatriptan), and no significant differences from placebo were reported for primary end points assessed. Several nonblinded anecdotal reports suggest triptans are effective, but clinical designs follow standard adult testing protocol. Migraine characteristics differ in children, suggesting that possibly different trial designs need to be considered.

MIGRAINE IN THE ELDERLY

- Be especially aware of secondary headaches
- Assess for coexistent disease
  - Coronary artery disease, hypertension
- Treatment
  - NSAIDs increase risk of AEs with age
  - Age alone is not a contraindication for triptans

Studies testing the efficacy of migraine medications specifically in the elderly have not been done. Medications have not been systematically studied for risks specifically in migraine patients. However, elderly patients should undergo the same, if not even more stringent, routine history, physical, and neurologic exam to rule out secondary causes of headache such as subarachnoid hemorrhage, stroke, or tumor. If the diagnosis is migraine, acute therapies include triptans, NSAIDs, and analgesics. Preventive therapies sometimes can be based on the presence of coexisting conditions, such as depression or high blood pressure. Elderly patients should be monitored routinely for improvement or deterioration in headache status, as well as for development of complications or confounding conditions.

PREVENTIVE TREATMENT

PREVENTIVE TREATMENT GOALS

- Reduce attack frequency, severity, and duration
- Improve responsiveness to treatment of acute attacks
- Improve function and reduce disability

PRINCIPLES OF PREVENTIVE CARE

- Recurrent migraines that, in the patient's opinion, significantly interfere with their daily routines, despite acute treatment
- Frequent headaches
- Contraindication to, failure of, or overuse of acute therapies
- AEs with acute therapies
- The presence of uncommon migraine conditions, including hemiplegic migraine, basilar migraine, migraine with prolonged aura, or migrainous infarction (to prevent neurologic damage—as based on expert consensus)

In the past, a common rule of thumb was that patients who experienced migraine two or more times per month were candidates for preventive therapy. That may remain an informal standard for thinking about preventive care, but patient perception of the need for preventive care has become the key consideration in making the decision. Keep in mind, though, that new information suggests that a frequency of 1 or more migraine a week is a risk factor for progression to CDH.

Because most medications used to treat migraine were developed for other indications, they can be frequently leveraged to optimize the care of more than one illness. For example, beta blockers can be used to treat migraine patients with coexistent high blood pressure, and tricyclic antidepressants can be used to treat migraine patients with comorbid depression. It is important to ensure that treatments being used for coexistent conditions do not exacerbate migraine.

PRINCIPLES OF PREVENTIVE TREATMENT

- Initiate therapy with the lowest effective dose, and increase the dose slowly until clinical benefits are achieved without AEs or until limited by AEs. This can be especially important when using antidepressants and neuroleptics; a long, slow ramp-up period will improve tolerability
- Give each treatment an adequate trial unless AEs preclude their continuation. Medications may take 2 to 3 months to demonstrate effectiveness
- Avoid interfering medications. Overuse of acute medications can impede the effectiveness of preventive medications. It is important to monitor and limit the use of acute medications. Use of long-acting formulations may improve compliance. In addition, patient education is critical to maximize compliance. The rationale for treatment, when and how to use it, and any possible AEs should be discussed. It is vital to set realistic expectations and useful to encourage patients to keep headache diaries so that progress can be measured. After a period of stability, it is useful to re-evaluate therapy and consider tapering or discontinuing treatment. Some preventive medications have teratogenic effects and their use should be avoided in women of childbearing age.

PREVENTIVE MEDICATIONS

SELECTED AGENTS USED IN PREVENTIVE TREATMENT OF MIGRAINE

See full prescribing information for complete list of AEs and contraindications for all medications listed.

Drug	Recommended Dose Starting Dose = SD; Maximum Dose = MD	Remarks
BETA BLOCKERS*		
Propranolol (Inderal®) 10/20/40/60/80 mg (Inderal LA®) 60/80/120/160 mg (Long-acting formula) Oral	SD: 40–80 mg/d MD: 400 mg/d	Efficacious doses in clinical trials: 80–240 mg/d. May be particularly helpful in patients with coexistent anxiety or panic attacks and essential tremors. When used in conjunction with rizatriptan, a lower dose of rizatriptan should be given. AEs may include drowsiness, lethargy, depression
Timolol (Blocadren®) 5/10/20 mg Oral	SD: 20 mg/d MD: 60 mg/d	Efficacious doses in clinical trials: 20–30 mg/d
Atenolol (Tenormin®) 25/50/100 mg Oral	SD: 50 mg/d MD: 200 mg/d	Efficacious doses in clinical trials: 100 mg/d
Metoprolol (Lopressor®) 25/50/100 mg (Toprol-XL®) 25/50/100/200 mg Long-acting formula Oral	SD: 100 mg/d MD: 200 mg/d SD: 100 mg/d MD: 200 mg/d	Efficacious doses in clinical trials: 200 mg/d
Nadolol (Corgard®) 20/40/80/120/160 mg Oral	SD: 20 mg/d MD: 160 mg/d	Efficacious doses in clinical trials: 80–240 mg/d
TRICYCLIC ANTIDEPRESSANTS (TCAs)		
Amitriptyline (Elavil®, Endep®) 10/25/50/75/100/150 mg Oral	SD: 10-25 mg/d MD: 150 mg/d	Efficacious doses in clinical trials: 30–150 mg/d; Drowsiness, weight gain, and anticholinergic AEs are common; long-term weight gain can be troublesome. Particularly useful in patients with migraine and tension-type headache (TTH) and in patients with coexistent depression. Risk of drug interaction between cisapride and amitriptyline. May lower seizure threshold in patients with frequent seizures

Drug	Recommended Dose Starting Dose = SD; Maximum Dose = MD	Remarks
Nortriptyline (Pamelor®, Aventyl®) 10/25/50/75 mg Oral	SD: 10-25 mg/d MD: 150 mg/d	Efficacious doses not established in clinical trials; better tolerated than amitriptyline
Protriptyline (Vivactil®) 5/10 mg Oral	SD: 15 mg/d MD: 40 mg/d	Efficacious doses not established in clinical trials; nonsedating and not as frequently associated with weight gain as other TCAs
Doxepin (Sinequan®, Adapin®) 10/25/50/75/100/150 mg Oral	SD: 50 mg/d MD: 150 mg/d	Efficacious doses not established in clinical trials
Imipramine (Tofranil®) 10/25/50/75/100/125/150 mg Oral	SD: 50 mg/d MD: 150 mg/d	Efficacious doses not established in clinical trials
NEUROMODULATORS		
Divalproex sodium (Depakote®) 125/250/500 mg delayed-release Divalproex sodium ER (Depakote ER®) 250/500 mg Oral	SD: 250 mg BID MD: 1 g/d For ER formulation: Initiate at 500 mg/d for 1 wk before advancing to 1000 mg/d taken once daily. Patients requiring smaller doses should use delayed-release formulation instead	Efficacious doses in clinical trials: 500–1500 mg/d; use low initial dose and titrate slowly; avoid abrupt cessation. Monitor liver function and clinical symptoms (especially for first 6 months). Apprise female patients of childbearing potential of risks to fetus (eg, neural tube defects). Re-evaluate periodically. Warn patients of symptoms of pancreatitis
Gabapentin (Neurontin®) 100/300/400 mg capsules 600/800 mg tablets Oral	SD: 300 mg TID MD: 2400 mg/d Doses of 3600 mg/d have been tolerated for brief periods	Efficacious doses in clinical trials: 900–2400 mg/d; see prescribing information for interactions with other migraine medications
Topiramate (Topamax®) 25/100/200 mg tablets 15/25 mg capsules Oral	Week 1: 15 mg bedtime Week 2: 15 mg BID Week 3: 15 mg AM, 30 mg bedtime Week 4: 30 mg AM, 45 mg bedtime Week 6: 45 mg BID Week 7: 50 mg BID	Emerging evidence suggests efficacy; slow ramp-up minimizes AEs. AEs: nausea and tingling of extremities, weight loss, fatigue, poor concentration

Drug	Recommended Dose Starting Dose = SD; Maximum Dose = MD	Remarks
SELECTIVE SEROTONIN REUPTAKE INHIBITORS (SSRIs)**		
Fluoxetine (Prozac®) 10/20/40 mg 90 mg (weekly) Oral	SD: 20 mg AM MD: 80 mg	Efficacious doses in clinical trials: 20 mg every other day to 40 mg/d; insomnia, fatigue, tremor, and stomach pain are the more common AEs. Consider use in patients with coexistent depression
Fluvoxamine (Brand disc.) 25/50/100 mg Paroxetine (Paxil®) 10/20/30/40 mg Sertraline (Zoloft®) 25/50/100 mg Oral		Efficacious doses not established in clinical trials
CALCIUM CHANNEL BLOCKERS***		
Verapamil (Calan®, Isoptin®) 120/180/240 mg extended-release 40/80/120 mg Oral	SD: 120 mg/d MD: 480 mg/d	Efficacious doses in clinical trials: 240 mg/d; constipation common; do not use if conduction block is present. Alternative to beta blockers in physically active people. Recommended in patients with coexistent stroke, or for prolonged or atypical migraine aura. Patient may feel drowsy or tired when first taking medication or when changing dose
Nimodipine (Nimotop®) 30 mg Oral	SD: 120 mg MD: 240 mg	Efficacious doses in clinical trials: 120 mg/d; abdominal discomfort common. Cost may be prohibitive
Diltiazem (Cardizem®) 30/60/90/120 mg 60/90/120/180/240/300 mg extended-release Oral	SD: 120 mg/d MD: 360 mg/d	Efficacious doses: not established in placebo-controlled clinical trials
Nifedipine (Procardia®) 10/20 mg 30/60 mg extended-release Oral	SD: 30 mg/d MD: 90 mg/d	Clinical trial results are ambiguous

Drug	Recommended Dose Starting Dose = SD; Maximum Dose = MD	Remarks
NSAIDS**		
Aspirin Oral	Various doses: 500 mg daily 325 mg every other day 200 mg daily	Efficacious doses tested in clinical trials: 1300 mg/d; high-dose aspirin may lead to overuse and development of rebound headaches. Common AEs include abdominal discomfort, gastritis, and occult GI bleed. May be useful for patients with arthritis. Consider aspirin in patients with coexistent stroke
Fenoprofen (Nalfon®) 200/300/600 mg Oral	SD: 200 mg MD: 1800 mg	Efficacious doses in clinical trials: 1800 mg/d
Flurbiprofen (Ansaid®) 50/100 mg Oral	SD: 50–100 mg MD: 300 mg	Efficacious doses in clinical trials: 200 mg/d
Mefenamic acid (Ponstel®) 250 mg Oral	SD: 500 mg followed by 250 mg q6h as needed MD: 1500 mg	Efficacious doses in clinical trials: 1500 mg/d; initiate with onset of menses; should not be necessary to take longer than 2–3 d
Naproxen sodium (Aleve®, Anaprox®) 250/375/500 mg Oral	SD: 550 mg MD: 1100 mg	Efficacious doses in clinical trials: 1100 mg/d
Ketoprofen (Orudis®/Oruvail®) 25/50/75 mg 100/150/200 mg controlled-release Oral	Orudis®: SD: 75 mg TID or 50 mg QID MD: 300 mg/d Oruvail®: SD: 200 mg MD: 200 mg	Efficacious doses in clinical trials: 150 mg/d
OTHER DRUGS		
Botulinum toxin A (Botox®) 50–150 units SC	2.5–7.5 units/site using tuberculin syringe 0.05–0.3 cc/injection site, approximately 15–20 sites	Emerging evidence exists in controlled and uncontrolled trials. Three strategies for injection: fixed-site, follow the pain, and combined. Usual sites include frontalis, temporalis, orbicularis oculi, procerus, splenius capitis, semispinalis capitis/upper trapezius

Drug	Recommended Dose Starting Dose = SD; Maximum Dose = MD	Remarks
Ergotamine† (Ercatab®) Oral	2 caps BID or at bedtime for 3 d before, during, and 2 d after menses	Prophylactic use of ergotamine is discouraged except for women with primarily menstrual migraine who can use it only at the time of headache vulnerability; Cafergot comp® taken BID during menses may reduce menstrually associated migraine; efficacious dose not established during clinical trials
Tizanidine (Zanaflex®) 4 mg Oral	Slowly titrate over 4 wk in 4-dose intervals SD: 1 mg at bedtime MD: 24 mg or maximum tolerated dose taken	Recent evidence suggests efficacy as an adjunct therapy for chronic daily headache (CDH); AEs reported include somnolence, dizziness, dry mouth, and asthenia
Magnesium Oral	400 mg	Efficacious doses in clinical trials: 400 mg/d; use of nonchelated formulation is associated with significant diarrhea at clinically effective doses. Magnesium hydroxide is NOT recommended because of poor bioavailability and high laxative effect. May be useful in patients with PMS
Riboflavin (Vitamin B_2) Oral		Efficacious doses in clinical trials: 400 mg/d; rare AEs; no known interaction with other drugs
Feverfew Oral		Efficacious doses in clinical trials: 10–30 mg/d; withdrawal of feverfew may be associated with increased headaches

*Beta blockers: AEs include tiredness, fatigue, and dizziness; may not be accepted by physically active patients; should not be used in patients with coexistent asthma, cardiac insufficiency, or Raynaud's disease. May exacerbate depression.

**SSRIs rarely interact with 5-HT agonists.

***Calcium channel blockers: AEs include dizziness and headache, depression, weight gain, vasomotor changes, tremor, GI complaints, peripheral edema, orthostatic hypotension, and bradycardia. Patients frequently report an initial increase in headache. Headache improvement frequently takes weeks of treatment.

****NSAIDs: Can be effective for short-term prophylactic therapy for menstrual migraine taken a few days before anticipated onset of menses and through period of risk for headache. They must otherwise be used with caution because of their AEs on GI and renal function.

†Ergotamine: Screen for asymptomatic cardiac disease in patients at risk. Potentiated by protease inhibitors, macrolides, azole antifungals, saquinavir (Invirase®), nefazodone (Serzone®), fluoxetine (Prozac®), fluvoxamine (Luvox®), zileuton (Zyflo®), propranolol (Inderal®), grapefruit juice, nicotine. Contraindicated in patients with risk of heart disease, basilar or hemiplegic migraine, or uncontrolled hypertension. Contraindicated with concomitant ritonavir (Norvir®), nelfinavir (Viracept®), indinavir (Crixivan®), erythromycin, clarithromycin (Biaxin®), troleandomycin (TAO), ketoconazole (Nizoral®), itraconazole (Sporonox®) or other vasoconstrictors.

Adapted from Davidoff RA. *Migraine: Manifestation, Pathogenesis, and Management.* Philadelphia, PA: FA Davis; 1995.

Ramadan NM, et al. Evidence-based guidelines for migraine headache in the primary care setting: pharmacological management for prevention of migraine. April 25, 2000. Available at: http://www.aan.com/professionals/practice/pdfs/gl0090.pdf. Accessed October 22, 2003.

Silberstein SD, Saper JR, Freitag FG. Migraine diagnosis and treatment. In: Silberstein SD, Lipton RB, Dalessio DJ, eds. *Wolff's Headache and Other Head Pain.* 7th ed. Oxford: Oxford University Press; 2001:121-237.

Physicians' Desk Reference®. Montvale, NJ: Medical Economics Company; 2003.

PREVENTIVE TREATMENT: COEXISTING CONDITIONS

Certain preventive treatments can be used to effectively treat comorbid conditions; on the other hand, certain preventive medications are contraindicated for use in patients with specific comorbid conditions. The chart below summarizes the use of preventive medications with specific comorbid conditions.

			Comorbid Condition	
Drug	**Efficacy***	**Side Effects***	**Relative Contraindication**	**Relative Indication**
Neuromodulators:				
Divalproex	4+	2+	Liver disease bleeding disorders	Mania, epilepsy, anxiety disorders
Gabapentin	2+	2+		Neuropathic pain
Topiramate	4+	2+	Kidney stones	Epilepsy, mania
Antidepressants:				
TCAs	4+	4+	Mania, urinary retention, heart block	Other pain disorders, depression anxiety disorders, insomnia
SSRIs	2+	2+	Mania	Depression, OCD
Beta blockers	4+	2+	Asthma, depression, CHF, Raynaud's disease, diabetes	HTN, angina
Calcium channel blockers:				
Verapamil	2+	1+	Constipation, hypotension	Migraine with aura, HTN, angina, asthma
NSAIDs:				
Naproxen	2+	2+	Ulcer disease, gastritis	Arthritis, other pain disorders
Other:				
Riboflavin	2+	1+		
Feverfew	2+	2+		Preference for natural products
Botulinum toxin A	2+	1+		

*Rating scales: Efficacy: 1=not effective; 4=very effective. Side effects: 1=minimal/no effects; 4=severe effects.
Adapted from Silberstein SD et al. *Cephalagia.* 2002; 22:491-512.

BEHAVIORAL THERAPIES

Behavioral therapies are an important adjunct to acute and preventive medical management of migraine. Most patients will require management with medication, but some will prefer nonpharmacologic interventions. Others will have poor tolerance for or medical contraindications to specific pharmacologic treatments. Some patients will have insufficient or no response to pharmacologic treatment. Women who are pregnant, nursing, or planning pregnancy will seek alternatives to pharmacologic management. A minority of patients will have a history of long-term, frequent, or excessive use of acute medications that have aggravated their headache problems. Some may be under significant stress or have inadequate stress coping skills for their situation. These patients will likely benefit from the inclusion of behavioral therapies in their treatment plan.

All patients benefit from behavioral strategies of improved diet, exercise, and lifestyle and stress management. Avoiding triggers, many of which are lifestyle related, can be an important component in reducing the frequency of migraine attacks. Relaxation training (eg, progressive muscle relaxation, meditation) teaches patients to control muscle tension and use mental relaxation and visual imagery to achieve treatment goals. Biofeedback is standard thermal (hand-warming) and electromyographically guided training. Cognitive behavioral therapy includes psychotherapeutic interventions that have as a primary goal teaching patients skills for identifying and controlling stress, as well as minimizing the effects of stress.

GOALS OF BEHAVIORAL THERAPY

- Reduce the frequency and severity of headache
- Reduce headache-related disability
- Reduce reliance on poorly tolerated or unwanted pharmacotherapies
- Enhance personal control of migraine
- Reduce headache-related distress and psychological symptoms

Sufficient high-quality evidence exists to recommend the following behavioral therapies for the nonpharmacologic treatment of migraine:

- Relaxation training
- Thermal biofeedback with relaxation training
- EMG biofeedback
- Cognitive behavioral therapy

Insufficient evidence exists to recommend the following therapies for the treatment of migraine:

- Acupuncture
- TENS (Transcutaneous Electrical Nerve Stimulation)
- Cervical manipulation
- Occlusal adjustment
- Hyperbaric oxygen
- Hypnosis

BEHAVIORAL STRATEGIES

- Avoid known triggers
- Lifestyle and stress management

Most headache patients can and should be cared for in primary care settings. In some situations, referral to a specialist with experience in treating complex headache problems or a specialty headache clinic may be the wisest course of action. Such situations may include

- A patient whose symptoms remain unchanged despite aggressive treatment, whose initial diagnosis is in question, or where there is physician or patient discomfort with the progress of therapy
- A patient whose level of disability persists or worsens despite treatment with medication in more than one class of medication
- A patient whose symptoms change or where diagnosis is unclear
- A patient with comorbid conditions that complicate treatment, such as coronary artery disease, renal failure, or hypertension
- A patient who is or becomes dependent upon medications, fails attempts at outpatient drug withdrawal, or whose rebound headaches make outpatient management impractical or unwise

WHEN TO REFER PATIENTS TO HEADACHE SPECIALISTS

For the majority of migraine sufferers, good care is provided in primary care centers and patients are managed on appropriate migraine-specific medications and preventive therapies. However, other patients have clear challenges and referral to a neurologist or a headache specialist is warranted. Some patients do not present with all the IHS-defined criteria for migraine with or without aura. There may be concerns of secondary headache or patients may have selected risk factors that make migraine more difficult to treat with triptans or standard headache therapies. Another reason to refer patients to tertiary care centers is when they are not responding to typical migraine treatments. These patients may be at risk of overusing medications. Lastly, migraine patients may have a higher incidence of coexisting conditions, such as depression, anxiety, obesity, hypertension, or a number of other health concerns. These patients may be more difficult to treat, as they may require close monitoring and polytherapy.

SUMMARY

Acute treatment goals

- Treat attacks quickly and consistently
- Avoid recurrence
- Restore functioning
- Minimize use of backup and rescue meds
- Eliminate or minimize AEs
- Optimize self-care and reduce subsequent need for resource use
- Provide cost-effective care

When planning treatment, consider

- Patient's age
- Current health status
- Coexisting illnesses
- Migraine type

Principles of acute treatment

- Enlist patient in therapeutic alliance
- Treat headache early in the attack
- Tailor treatment to both the individual and the specific attack
- Limit acute medications to two to three times per week
- Monitor medication use

Select medication based on

- Frequency
- Severity
- Disability
- Associated symptoms (eg, nausea)
- Previous response to therapy
- How quickly headache builds
- Duration
- Tendency for recurrences
- AEs
- Patient preference

Specific headache populations

- Menstrual migraine
- Migraine in children
- Migraine in elderly

Goals of preventive therapy

- Reduce attack frequency, severity, and duration
- Improve responsiveness to treatment of acute attacks
- Improve function and reduce disability

Preventive therapy should be used in patients who have

- Recurrent migraines that persist and significantly interfere with patient's daily routine despite treatment
- Frequent headaches
- Contraindication to, failure of, or overuse of acute therapies
- AEs with acute therapies
- Patient preference for preventive therapy

Key management concepts

- Initiate therapy with lowest effective dose and increase slowly until clinical benefit is achieved without AEs
- Give each treatment an adequate trial; medications may take 2 to 3 months to demonstrate effectiveness
- Avoid interfering medications—acute medications may impede effectiveness of preventive medications. Monitor and limit use of acute medications
- Use of long-acting formulations may improve compliance
- Patient education is critical to maximize compliance
- Encourage patients to keep headache diaries
- After a period of stability, re-evaluate therapy and consider tapering or discontinuing treatment

Behavioral therapy goals

- Reduce frequency and severity of headaches
- Reduce headache-related disability
- Reduce reliance on poorly tolerated or unwanted pharmacotherapies
- Enhance personal control of migraines
- Reduce headache-related distress and psychological symptoms

When to refer

- Patient's symptoms remain unchanged despite treatment efforts, initial diagnosis is in question, or physician or patient discomfort with progress of therapy exists
- Patient's level of disability worsens despite treatment
- Status of symptomatology changes, no longer fitting diagnostic criteria
- Comorbid conditions exist requiring special care or complex polypharmacy
- Patient is or becomes habituated, has failed attempts at detoxification, or rebound headaches limit outpatient management

Commonly Asked Questions

What behavior changes should I encourage and reinforce for my patients with migraine?

Irregular sleep and wake times, fasting, caffeine withdrawal, and alcohol are such common triggers for migraine that it makes sense to encourage their avoidance in most patients. Foods are headache triggers for some patients but overrated in most and are highly individual. It's important to encourage patients to try to identify headache triggers but not to become obsessed with trigger elimination, especially foods. Food elimination diets are usually unnecessary and can lead to an obsessive focus on diet that contributes to, rather than reduces, the burden of disease.

How do I decide which triptan to use?

It depends on the patient and the circumstances of their headache. Consider how quickly the headache builds, how long it lasts, whether it frequently recurs, whether the patient is particularly sensitive to AEs and patient preference. Several of the triptans come in more than one formulation. Efficacy differences among the triptans may be statistically small but of clinical importance for an individual patient. Patients who do not respond to one triptan or who experience AEs may do well with another. For example, sumatriptan given as a subcutaneous injection works rapidly, with some patients reporting a reduction in pain in 10 minutes and 70% to 73% reporting pain relief in 1 hour. Zolmitriptan and rizatriptan are available as rapidly dissolving tablets that begin to act within 30 minutes and are especially appreciated by patients who have no access to water, need a discreet method of taking medication, or have difficulty swallowing tablets. Naratriptan and frovatriptan have a slower onset of action than the other triptans but may have lower recurrence rates and be particularly helpful for migraine of long duration. Almotriptan, a newer triptan, may be helpful for patients who are especially sensitive to feelings of chest pressure and other AEs. The newest triptan, eletriptan, appears to have a high response rate and may work for migraine patients who have not responded to other triptans. Sumatriptan and zolmitriptan are now both available as nasal sprays.

Many migraine patients have other health problems. How does that affect selection of a preventive treatment for migraine?

It is sometimes possible for one drug to have a beneficial effect on both conditions. Propranolol can be an excellent choice for a migraine patient with high blood pressure. However, screening for comorbid depression is important because propranolol can aggravate depression. Beta blockers should be avoided for patients with asthma, diabetes, or Raynaud's disease. Many migraine experts also avoid their use in patients who have migraine with aura. A calcium channel blocker such as verapamil can also be considered. There is preliminary evidence that other blood pressure drugs, such as lisinopril or candesartan, may be useful for migraine prophylaxis as well. Amitriptyline or other TCAs can be useful for migraine patients with comorbid depression, anxiety, or sleep disturbance, as well as patients who have mixed migraine and TTH. Keep in mind that the doses of TCAs helpful in migraine may be too low to have an effect on depression, however. Migraine patients with epilepsy, anxiety, or bipolar disorder may benefit from divalproex sodium or topiramate. Unlike beta blockers, anticonvulsants can be administered safely to patients with depression, Raynaud's disease, asthma, and diabetes.

BIBLIOGRAPHY

Campbell JK, Penzien DB, Wall EM. Evidence-based guidelines for migraine headache: behavioral and physical treatments. April 25, 2000. Available at: http://www.aan.com/professionals/practice/pdfs/gl0089.pdf. Accessed February 7, 2003.

Lipton RB, Stewart WF, Stone AM, et al. Stratified care vs. step care strategies for migraine: the Disabilities in Strategies of Care (DISC) study. *JAMA.* 2000;284:2599-2605.

Matchar DB. Evidence-based guidelines for migraine headache: pharmacological management of acute attacks. April 25, 2000. Available at: http://www.aan.com/professionals/practice/pdfs/gl0087.pdf. Accessed February 3, 2003.

National Headache Foundation. Standards of Care for Headache Diagnosis and Treatment. Chicago, IL; 2001. For more information on headache causes and treatments, professional membership, or a complete copy of The Standards of Care for Headache Diagnosis and Treatment, call the National Headache Foundation at 1-888-NHF-5552 or visit the Web site at www.headaches.org.

Ramadan NM, et al. Evidence-based guidelines for migraine headache in the primary care setting: pharmacological management for prevention of migraine. April 25, 2000. Available at: http://www.aan.com/professionals/practice/pdfs/gl0090.pdf. Accessed February 4, 2003.

Rapoport AM, Sheftell FD. *Headache Disorders—A Management Guide for Practitioners*. Philadelphia, PA: WB Saunders; 1996.

Silberstein SD. Practice parameter: evidence-based guidelines for migraine headache (an evidence-based review): report of the Quality Standards Subcommittee of the American Academy of Neurology. *Neurology.* 2000;55:754-762.

Silberstein SD, Saper JR, Freitag FG. Migraine diagnosis and treatment. In: Silberstein SD, Lipton RB, Dalessio DJ, eds. *Wolff's Headache and Other Head Pain.* 7th ed. Oxford: Oxford University Press; 2001:121-237.

CONCLUSIONS

- Migraine is a common, biologically based, neurovascular disorder that can be debilitating. It carries a high personal cost to migraine sufferers and their families. Migraine costs society billions of dollars every year
- Secondary headache, although critically important to detect and treat, is rare
- Improved therapies provide excellent relief for most migraine sufferers
- Response to medication is highly individual and frequently requires some trial and error
- Stress aggravates migraine, and positive outcomes require lifestyle adjustments by patients
- A minority of patients do not respond to therapy and have frequent, severe headaches or headaches that have transformed to CDH, sometimes as a consequence of medication overuse
- The treatment plan has to be implemented within the context of the patient's life
- Try to get diagnosis and treatment right the first time. Migraine patient drop-out from care is high due to frustration, poor relief, and medication side effects
- Create a therapeutic alliance; be sensitive to and respond to patient preferences about medication and delivery routes
- Provide reassurance and support for positive change
- Patient education is essential. Help them understand that medication will help but they have to make the essential lifestyle changes to minimize the frequency and reduce the severity of the attacks
- Enlist your support staff and use available educational materials to reduce the time required
- ACHE has a selection of patient education materials and an excellent Web site at www.achenet.org
- Give patients an abortive medication to be taken at onset, a backup medication if the abortive underperforms, and a rescue medication to use when all else fails to prevent trips to the emergency department
- Aggressively manage medication usage. Check for frequency and amount of use. Make sure patients understand how to use medications properly. Make sure the rescue drug doesn't become the abortive, etc
- Consider prevention for patients with frequent or severe headaches as defined by them
- Most migraine patients can be managed effectively in primary care settings; occasionally, referral may be necessary

Remember what migraine is—

Recurrent (with stable pattern) + Moderate to Severe + Nausea + Aggravated by Physical Movement + Pulsating + Temporarily Disabling = Migraine When Neuroexam Is Normal

APPENDIX

EVIDENCE-BASED GUIDELINES FOR MIGRAINE HEADACHE

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On behalf of the US Headache Consortium

Migraine is a common headache disorder characterized by attacks of head pain and neurologic, gastrointestinal, and autonomic symptoms. About 18% of women and 6% of men have migraine; many go undiagnosed and undertreated.[1] Migraine is a well-understood neurobiologic disorder characterized by a genetically based enhanced sensitivity of the nervous system. The attack is associated with activation of the trigeminal-vascular system.

The multidisciplinary US Headache Consortium produced four guidelines: diagnostic testing (primarily neuroimaging studies), acute drug treatment, preventive drug treatment, and behavioral and physical treatments for migraine.[2] These guidelines have been published at www.aan.com.[3-6]

The International Headache Society classification system is used to classify migraine.[7] If atypical features are present, exclude secondary headaches and then determine if any other coexisting primary headache (eg, TTH) is present. Avoid diagnostic testing if it will not lead to a change in management. Electroencephalography is not useful in the routine evaluation of headache.[8,9]

NEUROIMAGING: RISK FACTORS FOR INTRACRANIAL PATHOLOGY

Nonacute headache: Dizziness or lack of coordination, history of localized neurologic signs or subjective numbness or tingling, and history of headache causing awakening from sleep (although this can occur with migraine and cluster headache). Consider in patients with

- Unexplained abnormal neurologic examination
- Atypical headache or headache features (or additional risk factor, such as immune deficiency). Not needed in migraine patients with a normal neurologic examination

Acute headache: Acute onset, occipitonuchal location, age >55 years, associated symptoms, and an abnormal neurologic examination.[10]

MIGRAINE TREATMENT

Migraine varies in frequency, duration, and disability among sufferers and between attacks. Link the intensity of care with the level of disability and associated symptoms such as nausea and vomiting (stratified care). Do not continue ineffective or poorly tolerated medication in a sequential and arbitrary manner (step care).

GENERAL PRINCIPLES OF MANAGEMENT

- **Establish a diagnosis**
- **Educate migraine sufferers about their condition.** Discuss the rationale for a particular treatment, how to use it, and what AEs are likely
- **Establish realistic patient expectations**

- **Allow patients to be involved in their management.** Encourage patients to use headache dianes to track days of disability or missed work, school, or family activities
- **Choose treatment based on the frequency and severity of attacks, the presence and degree of temporary disability, and associated symptoms, such as nausea and vomiting**
- **Create a formal management plan and individualize management.** Consider the patient's response to, and tolerance for, specific medications. Avoid acute headache medication escalation. Identify coexisting conditions (such as heart disease, pregnancy, and uncontrolled hypertension) as they may limit treatment choices
- **Encourage the patient to identify and avoid triggers**

ACUTE TREATMENT GOALS

1. Treat attacks rapidly and consistently, without recurrence, and with minimal or no AEs
2. Restore the patient's ability to function
3. Minimize the use of backup and rescue medications. (A rescue medication is used at home when other treatments fail; it permits the patient to achieve relief without the discomfort and expense of a visit to the physician's office or emergency department)
4. Optimize self-care and reduce subsequent use of resources

TO MEET THESE GOALS

- **Use specific drugs (triptans [naratriptan, rizatriptan, sumatriptan, and zolmitriptan], DHE, and in selected cases, ergotamine) in patients with moderate or severe migraine or whose mild to moderate headaches respond poorly to NSAIDs or combinations such as aspirin plus acetaminophen plus caffeine.** Failure to use an effective treatment promptly may increase pain, disability, and the impact of the headache. Acetaminophen, alone, is not recommended for migraine
- **NSAIDs (oral), combination analgesics containing caffeine, and isometheptene combinations are a reasonable choice** for mild to moderate migraine attacks or severe attacks that have been responsive in the past to similar NSAIDs or nonopiate analgesics. Ketorolac IM is an option of uncertain clinical efficacy
- **Select a nonoral route of administration for patients with migraine associated with severe nausea or vomiting.** Do not restrict antiemetics just to patients who are vomiting or likely to vomit
- **Use a self-administered rescue medication for patients whose severe migraine does not respond to (or fails) other treatments.** Prochlorperazine IV, IM, and PR; chlorpromazine IV; corticosteroids (dexamethasone or hydrocortisone)
  Limit and carefully monitor the use of opiates and butalbital-containing analgesics
- **Guard against medication-overuse headache ("rebound headache").** Frequent use of acute medications (ergotamine [not DHE], opiates, triptans, and simple and mixed analgesics containing butalbital, caffeine, or isometheptene) can cause medication-overuse headache. Limit acute therapy to two headache days per week on a regular basis. Use preventive therapy

PREVENTIVE TREATMENT

Preventive treatment is necessary when migraine has a substantial impact on patients' lives and the attacks have not responded to acute care, or when the attack frequency is so high that acute medications would be overused. The goals are to (1) reduce attack frequency, severity, and duration; (2) improve responsiveness to treatment of acute attacks; and (3) improve function and reduce disability. Migraine patients often try nonpharmacologic headache treatment before or concurrently with drug therapy. Relaxation training, thermal biofeedback combined with relaxation training, EMG biofeedback, and cognitive behavioral therapy may be used alone or combined with preventive drug therapy to achieve additional clinical improvement for migraine relief.

Use preventive therapies when (any of these)

- Migraine significantly interferes with the patients' daily routines, despite acute treatment
- Frequent headaches (>2/week)
- Contraindication to, or failure, side effects, or overuse of acute therapies
- Patient preference
- Presence of uncommon migraine conditions, including hemiplegic migraine, basilar migraine, migraine with prolonged aura, or migrainous infarction

Guide to preventive medication use

1. Use medications with the best evidence-based efficacy and fewest AEs
2. Take coexisting conditions into account:
    a. Select a drug that will treat all conditions, if possible
    b. Be sure that the coexistent disease is not a contraindication to the migraine treatment
    c. Be sure that the treatments used for coexistent conditions do not exacerbate migraine
    d. Beware of drug interactions
3. Start low and increase the dose slowly until clinical benefits are achieved in the absence of, or until limited by, AEs
4. Give the selected drug an adequate trial at adequate doses (2–3 months)
5. Avoid interfering medications (eg, overuse of acute medications)
6. A long-acting formulation may improve compliance
7. Monitor the patient's headache through a headache diary
8. Re-evaluate therapy. If controlled at 6 months, consider tapering or discontinuing treatment

Evidence-Based Grading of Migraine Therapies

TABLE 1: ACUTE THERAPIES FOR MIGRAINE

Group 1: Proven pronounced statistical and clinical benefit	Group 2: Moderate statistical and clinical benefit	Group 3: Statistically but not proven clinically, or clinically but not proven statistically, effective	Group 4: Proven to be statistically or clinically ineffective	Group 5: Clinical and statistical benefits unknown
Nonspecific	APAP/codeine PO	Butalbital/aspirin/ caffeine PO	APAP PO	Dexamethasone IV
APAP/aspirin/caffeine PO	Butalbital/aspirin/ caffeine/codeine PO	Ergotamine PO	Chlorpromazine IM	Hydrocortisone IV
Aspirin PO	Butorphanol IM	Ergotamine/caffeine PO		
Butorphanol IN	Chlorpromazine IM, IV	Metoclopramide IM, PR		
Ibuprofen PO	Diclofenac K, PO			
Naproxen sodium PO	Ergotamine/caffeine/ pentobarbital/bellafoline PO			
Prochlorperazine IV	Flurbiprofen PO			
Specific	Isometheptene CPD, PO			
Naratriptan PO	Ketorolac IM			
Rizatriptan PO	Meperidine IM, IV			
Sumatriptan SC, IN, PO	Methadone IM			
Zolmitriptan PO	Metoclopramide IV			
DHE SC, IM, IV, IN	Naproxen PO			
Dihydroergotamine SC, IM, IV ± antiemetic, IN	Prochlorperazine IM, PR			
DHE IV plus antiemetic				

APAP = Acetaminophen

Evidence-Based Grading of Migraine Therapies (cont.)

TABLE 2: PREVENTIVE THERAPIES FOR MIGRAINE

Group 1: Medium to high efficacy, good evidence; mild to mod AEs	Group 2: Lower efficacy, or limited evidence; mild to mod AEs	Group 3: Clinically efficacious (consensus and clinical experience), no scientific evidence of efficacy	Group 4: Medium to high efficacy, good evidence, but AE concerns	Group 5: No more efficacy than placebo
Amitriptyline	**ß-blockers**	**Antidepressants**	Methysergide	Acebutolol
Divalproex sodium	Atenolol	Doxepin		Carbamazepine
Propranolol	Metoprolol	Fluvoxamine		Clomipramine
Timolol	Nadolol	Imipramine		Clonazepam
	Ca-blockers	Mirtazapine		Clonidine
	Nimodipine	Nortriptyline		Indomethacin
	Verapamil	Paroxetine		Nicardipine
	NSAIDs	Protriptyline		Nifedipine
	Aspirin	Sertraline		Pindolol
	Fenoprofen	Trazodone		
	Flurbiprofen	Venlafaxine		
	Ketoprofen	**Other**		
	Mefenamic acid	Cyproheptadine		
	Naproxen	Diltiazem		
	Naproxen sodium	Ibuprofen		
	Other	Tiagabine		
	Fluoxetine	Topiramate		
	Gabapentin	**AE concerns**		
	Feverfew	Methylergonovine		
	Magnesium	Phenelzine		
	Vitamin B_2			

References

1. Stewart WF, Lipton RB, Celentano DD, Reed ML. Prevalence of migraine in the United States. *JAMA.* 1992:267:64-69.
2. Silberstein SD, Rosenberg J. Multispecialty consensus on diagnosis and treatment of headache. *Neurology.* 2000;54:1553.
3. McCrory DC, Matchar DB, Rosenberg JH, Silberstein SD. Evidence-based guidelines for migraine headache: overview of program description and methodology. Available at: http://www.neurology.org.
4. Matchar DB, Young WB, Rosenberg JA, et al. Evidence-based guidelines for migraine headache in the primary care setting: pharmacological management of acute attacks. Available at: http://www.aan.com.
5. Frishberg B, Rosenberg JH, Matchar DB, et al. Evidence-based guidelines in the primary care setting: neuroimaging in patients with nonacute headache (in preparation). Available at: http://www.aan.com.
6. Campbell JK, Penzien D, Wall EM. Evidence-based guidelines for migraine headache: behavioral and physical treatments. Available at: http://www.neurology.org.
7. Ramadan NM, Silberstein SD, Freitag FG, et al. Evidence-based guidelines for migraine headache in the primary care setting: pharmacological management for prevention of migraine. Available at: http//www.neurology.org.
8. Headache Classification Committee of the International Headache Society. Classification and diagnostic criteria for headache disorders, cranial neuralgia, and facial pain. *Cephalalgia.* 1988;8(suppl 7):1-96.
9. Practice parameter: the electroencephalogram in the evaluation of headache (summary statement). Report of the Quality Standards Subcommittee of the American Academy of Neurology. *Neurology.* 1995;45:1411-1413.
10. Ramirez-Lassepas M, Espinosa CE, Cicero JJ, et al. Predictors of intracranial pathologic findings in patients who seek emergency care because of headache. *Arch Neurol.* 1997;54:1506-1509.

Patient Treatment Plan

Name _____

To optimize the management of your headaches, it is essential that you have a good understanding of the medications being prescribed to you. Our goal is to decrease the frequency of your headaches and to provide you with acute relief of pain when your headaches occur. Sometimes, medications do not work as anticipated and so a fall-back plan or rescue medication is often prescribed in addition to the preventive and acute medications. The following outlines your current treatment plan as provided by your physician.

❒ **Acute medication**

Definition: Acute medication reverses or stops the progression of a headache. It aborts a headache.

Dose 1 _____

Dose 2 _____

Max dose _____

❒ **Backup medication**

Definition: A different treatment taken when initial treatment fails or provides incomplete relief of headache.

Dose 1 _____

Dose 2 _____

Max dose _____

❒ **Rescue medication**

Definition: A potent drug taken only when other treatments fail to relieve severe headache.

Dose 1 _____

Dose 2 _____

Max dose _____

❒ **Preventive medication**

Definition: A treatment used on a daily basis, whether or not headaches are present, to decrease the frequency and severity of headaches.

Dose 1 _____

Dose 2 _____

Max dose _____

❒ **Lifestyle modification**

Definition: Changes made in habits and activities in daily living to help prevent headache.

Limit caffeine ____

Exercise ____

Avoid alcohol ____

Sleep ____

Use diary ____

GOALS OF TREATMENT

_____

_____

_____

_____

INTERNATIONAL HEADACHE SOCIETY, ICD-10 GUIDE FOR HEADACHES

General Notes

1. The criteria are labeled with letters and/or numbers to indicate their place in a hierarchy of generality and importance. General criteria, which must be fulfilled by all members of a group of disorders (such as the general criteria for all varieties of migraine with aura), are labeled with a capital G, plus a number. Obligatory criteria for individual disorders are distinguished by capital letters alone (A, B, C, etc), and lowercase letters (a, b, c, etc) are used to identify further groups and subgroups of characteristics, only some of which are required for the diagnosis.

2. To avoid the use of 'and/or', when it is specified that either of two criteria is required, it is always assumed that the presence of both criteria also satisfies the requirement.

3. When there is criterion that specifies frequency of attacks, lifetime should be taken into account, unless it is specified differently.

4. If the patient has more than one headache disorder, all should be diagnosed in the order of importance indicated by the patient.

5. After each diagnosis, the estimated number of headache days per year should be added in parentheses.

6. Patients who for the first time develop a particular form of headache in close temporal connection with the onset of one of the disorders listed in G44.3 (chronic post-traumatic headache), G44.4 (drug-induced headache), G44.8 (other specified headache syndromes), or G50–G53 (cranial neuralgia) (groups 5–11 of the IHS Classification, see Section III) are coded to these groups using additional characters to specify the etiology and additional codes to specify the type of the headache. Pre-existing migraine, TTH, or cluster headache aggravated in close temporal connection with one of the disorders listed in G44.3, G44.4, G44.8, or G50–G53 are still coded as migraine, TTH, or cluster headache (groups 1–3 of the IHS Classification). If the number of headache days increases by 100% or more, the aggravating factor may be mentioned in parentheses, but there is no separate code provided for its recording.

7. Code to the degree of specificity (number of characters) that suits your purpose.

8. If a patient has a form of headache fulfilling one set of diagnostic criteria, similar episodes that do not quite satisfy the criteria also usually occur. This can be due to treatment, lack of ability to remember symptoms exactly, and other factors. Ask the patient to describe a typical untreated attack or an unsuccessfully treated attack and ascertain that there have been enough of these attacks to establish the diagnosis. Then estimate the days per year with this type of headache adding also-treated attacks and less typical attacks.

9. A major obstacle to an exact diagnosis is the reliance on patients' history to determine whether criteria are met. In less clear cases, it is recommended letting the patient record attack characteristics prospectively using a headache diary before the diagnosis is made.

10. As already mentioned in the introduction, use of multiple coding is encouraged in all cases where there is a need to describe more extensively the different aspects of the patient's complaints. For instance, a depressed patient with headache would receive two codes, one for the type of headache and another one for the depression (F32) (see also list of commonly used additional categories, Section II).

Diagnostic Criteria

G43 Migraine

Use additional external cause code, if desired, to identify drug if drug-induced.
Excludes: headache NOS (R51), atypical facial pain (G50.1)

G43.0 Migraine without aura (common migraine)

Previously used terms: hemicrania simplex

Diagnostic criteria

A. There have been at least five attacks fulfilling criteria B, C, and D listed below
B. The headache attacks last between 4 and 72 h (untreated or unsuccessfully treated). Note: In children below age 15, attacks may last between 2 and 48 h. If the patient falls asleep and wakes up without migraine, the duration of the attack is until time of awakening
C. At least two of the following pain characteristics are present:
    1. Unilateral location
    2. Pulsating quality
    3. Moderate or severe intensity, inhibiting or prohibiting daily activities
    4. Aggravation by walking stairs or similar routine physical activity
D. At least one of the following symptom groups is present during the attack:
    1. Either nausea or vomiting
    2. Both photophobia and phonophobia
E. At least one of the following applies:
    1. History, physical, and neurologic examinations do not suggest one of the disorders listed in G44.3, G44.4, G44.8, or cranial neuralgia (G50–G53) (groups 5–11 of the IHS Classification, see Section III)
    2. History, physical, or neurologic examinations do suggest such a disorder, but it is ruled out by appropriate investigations
    3. Such a disorder is present, but the migraine attacks do not occur for the first time in close temporal connection with the disorder

Comments

Migraine without aura may occur almost exclusively at a particular time of the menstrual cycle—so-called menstrual migraine. Generally accepted criteria for this entity are not available. It seems reasonable to demand that 90% of attacks should occur between 2 days before menses and the last day of menses, but further epidemiologic knowledge is needed. Menstrual migraine should be coded N94.3 (Premenstrual tension syndrome) with code G43.0 in addition

G43.1 Migraine with aura (classic migraine)

Previously used terms: classic migraine, hemiplegic migraine accompagnée

Diagnostic criteria

G1. There have been at least two attacks fulfilling criterion G2 listed below

G2. At least three of the following characteristics are present:
1. There are one or more fully reversible aura symptoms indicating focal cerebral cortical or brain stem dysfunction
2. *Either* at least one aura symptom develops gradually over more than 4 min, or two or more symptoms occur in succession
3. The duration of the aura symptoms does not exceed 60 min
4. The headache follows the aura with a free interval of less than 60 min (it may also begin before or simultaneously with the aura)

G3. At least one of the following applies:

1. History, physical, and neurologic examinations do not suggest one of the disorders listed in G44.3, G44.4, G44.8, or cranial neuralgia (G50–G53) (groups 5–11 of the IHS Classification, see section III)
2. History, physical, or neurologic examination does suggest such a disorder, but it is ruled out by appropriate investigations
3. Such a disorder is present, but migraine attacks do not occur for the first time in close temporal connection with the disorder

G43.10 Migraine with typical aura

Diagnostic criteria

A. The general criteria for G43.1 are fulfilled

B. No aura symptom lasts more than 60 min; if more than one aura symptom is present, the accepted duration is proportionally increased

C. One or more of the following types of aura symptoms are present:

   1. Homonymous visual disturbance
   2. Unilateral paresthesias and/or numbness
   3. Unilateral weakness
   4. Aphasia or unclassifiable speech difficulty

G43.11 Migraine with prolonged aura

Diagnostic criteria

A. The general criteria for G43.1 are fulfilled

B. At least one aura symptom lasts more than 60 min, but not more than 7 days

G43.12 Migraine with acute onset aura

Diagnostic criteria

A. The general criteria for G43.1 are fulfilled

B. Neurologic symptoms develop suddenly (in less than 4 min from the onset of the headache)

C. The headache lasts between 4 and 72 h (untreated or unsuccessfully treated)

D. At least two of the following pain characteristics are present:

   1. Unilateral location
   2. Pulsating quality
   3. Moderate or severe intensity, inhibiting or prohibiting daily activities
   4. Aggravation by walking stairs or similar routine physical activity

E. At least one of the following symptom groups is present during the attack:

   1. Either nausea or vomiting
   2. Both photophobia and phonophobia

F. A transient ischemic attack (TIA) and other intracranial lesions are ruled out by appropriate investigations

To identify the neurologic symptoms in G43.1 Migraine with aura, a sixth character may be used, if desired, for categories G43.10, G43.11, and G43.12, as follows:

G43.1x0 Hemianoptic and other visual migraine

Previously used term: ophthalmic migraine

G43.1x1 Hemisensory migraine

Previously used term: hemiparesthetic migraine

G43.1x2 Migraine with aphasia

Previously used term: aphasic migraine

G43.1x3 Basilar migraine

Previously used terms: basilar artery migraine, Bickerstaff's migraine, syncopal migraine

Diagnostic criteria

A. The general criteria for G43.1 are fulfilled

B. Two or more aura symptoms of the following types are present:

1. Visual symptoms in both the temporal and nasal fields of both eyes
2. Dysarthria
3. Vertigo
4. Tinnitus
5. Decreased hearing
6. Double vision
7. Ataxia
8. Bilateral paresthesias
9. Bilateral pareses
10. Decreased level of consciousness

G43.1x4 Migraine aura (all types) without headache

Previously used term: acephalgic migraine

Diagnostic criteria

A. The general criteria for G43.1 are fulfilled

B. There is no headache

G43.1x5 Familial hemiplegic migraine

Diagnostic criteria

A. The general criteria for G43.1 are fulfilled

B. The aura includes some degree of hemiparesis and may be prolonged

C. At least one first-degree relative has identical attacks

G43.1x6 Multiple types of aura

G43.1x7 Other specified migraine with aura

G43.2 Status migrainosus

Diagnostic criteria

A. Either the criteria for G43.0 or the general criteria for G43.1 are fulfilled

B. The attack lasts more than 72 h whether treated or not

C. The headache is continuous throughout the attack or interrupted by headache-free intervals lasting less than 4 h. Note: Interruption during sleep is disregarded

G43.3 Complicated migraine

Previously used term: migrainous cerebral infarction

Diagnostic criteria

A. The general criteria for G43.1 have been fulfilled previously

B. The present attack is typical of previous attacks, but neurologic deficits are not completely reversible within 7 days, or neuroimaging demonstrates ischemic infarction in the relevant area of the brain

C. Other causes of infarction are ruled out by appropriate investigations

G43.8 Other migraine

G43.80 Ophthalmoplegic migraine

Diagnostic criteria

A. There have been at least two attacks fulfilling criterion B listed below

B. Headache associated with paresis of at least one of cranial nerves III, IV, or VI

C. Parasellar lesion has been ruled out by appropriate investigations

G43.81 Retinal (monocular) migraine

Diagnostic criteria

A. There have been at least two attacks fulfilling criteria B and C listed below

B. There is a fully reversible monocular scotoma or blindness or blindness lasting less than 60 min during an attack. This must be confirmed by examination during an attack or (after proper instruction) by patients' drawing of monocular field defect

C. Headache follows the visual symptoms with a free interval of less than 60 min, but may precede them

D. Ophthalmologic examination outside the attack is normal; embolism has been ruled out by appropriate investigations

G43.82 Childhood periodic migraine syndromes

G43.820 Abdominal migraine

Includes: migraine equivalents

Comments:

It is not possible to propose criteria for delineation of the multiple heterogeneous and undefined disorders comprised under the terms periodic syndromes, abdominal migraine, and cyclical vomiting, and it is unlikely that any progress will be made in this uncertain area until markers are found. At the present time, therefore, these syndromes of childhood cannot be included in the Classification despite the generally accepted view that some presentations are indeed headache-free "equivalents" of migraine

G43.821 Benign paroxysmal vertigo of childhood

Diagnostic criteria

A. There are multiple, brief, sporadic episodes of disequilibrium, anxiety, and often nystagmus or vomiting

B. Neurologic examination reveals no abnormalities

C. The electroencephalogram is normal

G43.822 Alternating hemiplegia of childhood

Diagnostic criteria

A. The onset is before 18 months of age

B. There are repeated attacks of hemiplegia involving both sides of the body

C. There are other paroxysmal phenomena, such as tonic convulsions, dystonic posturing, choreoathetoid movements, nystagmus or other ocular motor abnormalities, or autonomic dysbalances associated with the bouts of hemiplegia or occurring independently

D. There is evidence of a mental or neurologic deficit

G43.83 Atypical migraine

Diagnostic criteria

A. All criteria but one are fulfilled of one or more forms of migraine (specify type[s])

B. The criteria for TTH (G44.2) are not fulfilled

G43.9 Migraine, unspecified

This is a nonrecommended residual category, to be employed when no other code from this classification can be used. The terms "cyclic migraine," "lower half headache," "facial migraine," "hemicrania continua," and "cervical migraine" are not sufficiently validated

G44 Other headache syndromes

Excludes: typical facial pain (G50.1)
glossopharyngeal neuralgia (G52.1)
headache NOS (R51)
post-lumbar puncture headache (G97.0)
trigeminal neuralgia (G50.0)
other cranial neuralgias (G52.8)

G44.0 Cluster headache syndrome

Previously used terms: Erythroprosopalgia of Bing, ciliary or migrainous neuralgia [Harris], erythromelalgia of the head, Horton's headache, histaminic cephalalgia, petrosal neuralgia [Gardner], sphenopalatine, Vidian and Sluder's neuralgia, hemicrania periodica neuralgiformis

Diagnostic criteria

G1. There have been at least five attacks fulfilling criteria G2, G3, and G4

G2. There is severe unilateral orbital, supraorbital, or temporal pain lasting between 15 and 180 min, untreated

International Headache Society complete guidelines located at http://i-h-s.org

GUIDELINES FOR TERMINATING USE OF PRESCRIPTION ANALGESICS

Many patients with recurrent headaches take too many analgesics too often in an effort to relieve their pain. Ironically, this overuse contributes to the problem through "analgesic rebound headaches" and not until patients are weaned off medications do their headaches improve.

Mixed butalbital compounds

- Calculate average daily butalbital intake (50 mg per tablet)
- Reduce daily intake by 1 tablet q3–5d or convert 100 mg short-acting butalbital to its phenobarbital equivalent (100 mg butalbital = 30 mg phenobarbital)
- Give in divided doses
- Taper 10% to 15% q2–4d
- Adjust caffeine content when appropriate
- Monitor for sedation or central nervous system irritability
- Monitor for potential interactions with preventive medications

Mixed butalbital compounds with codeine

- For butalbital, follow procedure above
- Reduce codeine by 30 mg QD
- Consider use of clonidine HCl, given orally (0.05 or 0.1 mg TID) or in transdermal patches (2.5 or 5 mg total clonidine content)
- Consider use of naltrexone HCl* 50 mg QD (or TID for faster withdrawal)

Opioids

- Reduce by 1 tablet or spray QD or q3–4d
- Consider use of clonidine or naltrexone*
- Treat sleep disturbance with tricyclic antidepressant, trazodone HCl, or hydroxyzine

Benzodiazepines

- Reduce slowly, by 1/2 tablet q7d
- Differentiate among withdrawal, recurrence of original symptoms, and rebound
- Consider use of carbamazepine to speed tapering

Ergotamine tartrate

- Reduce by 0.5 to 1 mg QD
- Consider use of clonidine

*Naltrexone is an opioid antagonist that may cause withdrawal in patients dependent on opioids.

Rapoport AM, Sheftell FD. *Headache Disorders—A Management Guide for Practitioners.* Philadelphia, PA: WB Saunders; 1996.

Headache Organizations and Resources

AMERICAN HEADACHE SOCIETY (AHS)
19 Mantua Road
Mount Royal, NJ 08061
Phone: 856-423-0043
Fax: 856-423-0082
http://www.ahsnet.org

AMERICAN COUNCIL FOR HEADACHE EDUCATION (ACHE)
19 Mantua Road
Mount Royal, NJ 08061
Phone: 856-423-0258
Fax: 856-423-0082
http://www.achenet.org

AMERICAN ACADEMY OF NEUROLOGY (AAN)
1080 Montreal Avenue
Saint Paul, MN 55116
Phone: 651-695-2717
Fax: 651-695-2791
http://www.aan.com

INTERNATIONAL HEADACHE SOCIETY (IHS)
Oakwood
9 Willowmead Drive
Cheshire
SK10 4BU, UK
Phone: +44 (0) 1625 828663
Fax: +44 (0) 1625 828494
http://i-h-s.org

NATIONAL HEADACHE FOUNDATION (NHF)
820 N. Orleans, Suite 217
Chicago, IL 60610
Phone: 888-643-5552
Fax: 773-525-7357
http://www.headaches.org

MIGRAINE AWARENESS GROUP:
A National Understanding of Migraineurs (M.A.G.N.U.M.)
113 South Saint Asaph, Suite 300
Alexandria, VA 22314
Phone: 703-739-9384
Fax: 703-739-2432
http://www.migraines.org

WORLD HEADACHE ALLIANCE
3288 Old Coach Road
Burlington
Ontario
Canada, L7N 3P7
http://www.w-h-a.org
mail@w-h-a.org

Glossary of Terms

Acute medications	Medications that have a short and relatively severe duration; medications that are less suitable for repeat prescription; for occasional use
Behavioral therapy	Nonmedicinal therapies such as progressive relaxation, biofeedback, and stress management
Biofeedback	Behavior training program for headache (or other conditions) that teaches a person how to control certain autonomic reactions such as heart rate, blood pressure, skin temperature, and muscular tension
Central sensitization	Increased likelihood of firing in certain areas of the brain (for example, as a result of reduced threshold for action potentials) in response to repeated nerve stimulation
Chronic daily headache (CDH)	Headache in patients with one of a group of primary headache disorders (such as migraine or tension-type headache) that has evolved from episodic to chronic migraine or chronic tension-type headache
Chronic medications	Medications with enough efficacy to control most or all headaches (or other conditions) over an indefinite period, with an acceptably safe record of adverse events when taken over the long term
Cognitive behavioral therapy	An approach to psychotherapy that helps patients take control of their illness, and their lives, through insight, self-knowledge, and planning and using this new awareness to reduce unhealthy behaviors and to practice healthier new habits
Comorbid conditions	When one or more conditions occur at the same time; dual diagnosis
Cortical spreading depression (CSD)	Relatively short-lasting wave of depolarization that spreads across the surface of the brain, moving from the back (occipital region) of the cerebral cortex toward the front at about 3–5 mm/minute; may be underlying mechanism of migraine aura
Cutaneous allodynia	Hypersensitivity to touch so that normally unremarkable stimuli are very painful
Dopamine D2 receptor gene	Analyzed as a candidate gene for the cause of migraine. Antagonists of this receptor have been reported to be effective in the acute treatment of migraine; plays a modifying role in the pathophysiology of migraine with aura
Familial hemiplegic migraine (FHM)	Rare disorder found in families where two or more people suffer migraine-type headache associated with a "stroke-like" aura of weakness on one side of the body. Other neurologic symptoms can also occur and might include visual loss, difficulty with speech, confusion, and numbness. In these families, hemiplegic migraine has an autosomal dominant inheritance pattern, meaning that if either the mother or father has the gene and passes it on, that child will have hemiplegic migraine
Medication overuse	Use of acute medications for migraine on a daily or near daily basis; may lead to chronic/rebound headache
Menstrual migraine	The term "pure menstrual migraine" or "true menstrual migraine" refers to migraine attacks that occur only with menses. If attacks occur mainly, but not exclusively with menses, this may be referred to as "mainly menstrual migraine"

Migraine	One of the more common types of headache. This type of headache, due to changes in the brain and surrounding blood vessels, leads to pain and associated symptoms such as nausea, vomiting, light/sound sensitivity, and the "aura" of migraine
Migraine with aura	Aura is a neurologic symptom that develops over 5 to 20 minutes and usually lasts less than 60 minutes. It may consist of seeing flashing lights or curved lines, arm or leg numbness or tingling, or rarely one-sided weakness, or language difficulties
Migraine without aura	Most common type of migraine; migraine of sudden onset, without an early symptom indicating attack
Phonophobia	Abnormal sensitivity to sound
Photophobia	Abnormal sensitivity to light
Prevalence	The number of cases of a disease that are present in a population at one point in time
Preventive treatment	Intended to reduce the suffering and disability associated with attacks. Unfortunately, preventive treatment strategies rarely eliminate migraine, but they can reduce the frequency and severity of attacks. Can be achieved through a combination of education, lifestyle changes, and therapies (pharmacologic and nonpharmacologic)
Primary headache	Actual clinical condition and not a symptom of or caused by another disorder. Includes migraines, tension-type headache, and cluster headache
Relaxation training	Nonpharmacologic approach that involves taking slow, deep breaths, focusing the mind on a relaxing image or scene, and using soft relaxing lighting and sounds; begins with two primary techniques of abdominal or deep breathing and progressive muscle relaxation
Secondary headache	Caused by other medical conditions such as sinus disease, allergies, dental disorders, head injury, or brain tumors
Sinus headache	Caused by sinus infections or some other irritation inside the sinus cavities; also known as sinus-related headache
Tension-type headache (TTH)	Previously called muscle tension, contraction, or stress headache; most common type of headache in the general population, but most sufferers do not seek medical attention
Thunderclap headache	Sudden onset of a severe headache that reaches peak intensity in less than 1 minute. Thunderclap headache is usually benign but may be indicative of subarachnoid hemorrhage or another serious intracranial disorder
Triggers	Anything that can set off a migraine headache in a genetically predisposed individual. Common triggers include (but are not limited to) stress; changes in female hormone levels; skipping meals; certain odors, such as perfume; sleeping late on weekends; sleep loss; alcohol; and some foods including cheese, chocolate, and MSG
Triptans	Selective serotonin 5-$HT_{1B/1D}$ receptor agonists; effective acute migraine drugs; bind to serotonin (5-hydroxy-tryptamine) receptors in the brain, where they act to induce vasoconstriction of extracerebral blood vessels and also reduce neurogenic inflammation