Migraine

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(See also Approach to the Patient With Headache.)

Migraine is an episodic primary headache disorder. Symptoms typically last 4 to 72 h and may be severe. Pain is often unilateral, throbbing, worse with exertion, and accompanied by symptoms such as nausea and sensitivity to light, sound, or odors. Auras occur in about 25% of patients, usually just before but sometimes after the headache. Diagnosis is clinical. Treatment is with triptans, dihydroergotamine, antiemetics, and analgesics. Preventive regimens include lifestyle modifications (eg, of sleeping habits or diet) and drugs (eg, beta-blockers, amitriptyline, topiramate, divalproex).

Epidemiology

Migraine is the most common cause of recurrent moderate to severe headache; 1-yr prevalence is 18% for women and 6% for men in the US. Migraine most commonly begins during puberty or young adulthood, waxing and waning in frequency and severity over the ensuing years; it often diminishes after age 50. Studies show familial aggregation of migraine.

Evidence based on evaluation of veterans of the Iraq and Afghanistan conflicts suggests that migraine may frequently develop after mild traumatic brain injury.

Pathophysiology

Migraine is thought to be a neurovascular pain syndrome with altered central neuronal processing (activation of brain stem nuclei, cortical hyperexcitability, and spreading cortical depression) and involvement of the trigeminovascular system (triggering neuropeptide release, which causes painful inflammation in cranial vessels and the dura mater).

Many potential migraine triggers have been identified; they include the following:

- Drinking red wine
- Skipping meals
- Excessive afferent stimuli (eg, flashing lights, strong odors)
- Weather changes
- Sleep deprivation
- Stress
- Hormonal factors, particularly menstruation
- Certain foods

Head trauma, neck pain, or temporomandibular joint dysfunction sometimes triggers or exacerbates migraine.

Fluctuating estrogen levels are a potent migraine trigger. Many women have onset of migraine at menarche, severe attacks during menstruation (menstrual migraine), and worsening during menopause. For most women, migraines remit during pregnancy (but sometimes they worsen during the 1st or 2nd trimester); they worsen after childbirth, when estrogen levels decrease rapidly.

Oral contraceptives and other hormone therapy occasionally trigger or worsen migraine and have been associated with stroke in women who have migraine with aura.

Familial hemiplegic migraine, a rare subtype of migraine, is associated with genetic defects on chromosomes 1, 2, and 19. The role of genes in the more common forms of migraine is under study.

Symptoms and Signs

Often, a **prodrome** (a sensation that a migraine is beginning) heralds attacks. The prodrome may include mood changes, loss of appetite, nausea, or a combination.

An **aura** precedes attacks in about 25% of patients. Auras are temporary neurologic disturbances that can affect sensation, balance, muscle coordination, speech, or vision; they last minutes to an hour. The aura may persist after headache onset. Most commonly, auras involve visual symptoms (fortification spectra—eg, binocular flashes, arcs of scintillating lights, bright zigzags, scotomata). Paresthesias and numbness (typically starting in one hand and marching to the ipsilateral arm and face), speech disturbances, and transient brain stem dysfunction (causing, for example, ataxia, confusion, or even obtundation) are less common than visual auras. Some patients have an aura with little or no headache.

Headache varies from moderate to severe, and attacks last from 4 h to several days, typically resolving with sleep. The pain is often unilateral but may be bilateral, most often in a frontotemporal distribution, and is typically described as pulsating or throbbing.

Migraine is more than a headache. Associated symptoms such as nausea (and occasionally vomiting), photophobia, sonophobia, and osmophobia are prominent. Patients report difficulty concentrating during attacks. Routine physical activity usually aggravates migraine headache; this effect, plus the photophobia and sonophobia, encourages most patients to lie in a dark, quiet room during attacks. Severe attacks can be incapacitating, disrupting family and work life.

Attacks vary significantly in frequency and severity. Many patients have several types of headache, including milder attacks without nausea or photophobia; they may resemble tension-type headache but are a forme fruste of migraine.

Chronic migraines

Patients with episodic migraine can develop chronic migraine. These patients have headaches ≥ 15 days/mo. This headache disorder used to be called combination or mixed headache because it had features of migraine and tension-type headache. These headaches often develop in patients who overuse drugs for acute treatment of headaches.

Other symptoms

Other, rare forms of migraine can cause other symptoms:

- **Basilar artery migraine** causes combinations of vertigo, ataxia, visual field loss, sensory disturbances, focal weakness, and altered level of consciousness.
- **Hemiplegic migraine,** which may be sporadic or familial, causes unilateral weakness.

Diagnosis

- Clinical evaluation

Diagnosis of migraine is based on characteristic symptoms and a normal physical examination, which includes a thorough neurologic examination.

Red flag findings that suggest an alternate diagnosis (even in patients known to have migraine) include the following:

- Pain that reaches peak intensity within a few seconds or less (thunderclap headache)
- Onset after age 50
- Headaches that increase in intensity or frequency for weeks or longer
- History of cancer (brain metastases) or an immunosuppressive disorder (eg, HIV infection, AIDS)
- Fever, meningismus, altered mental status, or a combination
- Persistent focal neurologic deficits
- Papilledema
- A clear change in an established headache pattern

Patients with characteristic symptoms and no red flag findings do not require testing. Patients with red flag findings often require brain imaging and sometimes lumbar puncture.

Common diagnostic errors include the following:

- Not realizing that migraine often causes bilateral pain and is not always described as throbbing
- Misdiagnosing migraine as sinus headache or eyestrain because of autonomic and visual symptoms of migraine
- Assuming that any headache in patients known to have migraine represents another migraine attack (a thunderclap headache or a change in the previous headache pattern may indicate a new, potentially serious disorder)
- Mistaking migraine with aura for a transient ischemic attack, especially when the aura occurs without headache, in older people
- Diagnosing a thunderclap headache as migraine because a triptan relieves it (a triptan can also relieve a headache due to subarachnoid hemorrhage)

Several unusual disorders can mimic migraine with aura:

- Dissection of the carotid or vertebral artery
- Cerebral vasculitis
- Moyamoya disease
- CADASIL (cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy)
- MELAS (mitochondrial encephalopathy, lactic acidosis, and strokelike episodes) syndrome

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Prognosis

For some patients, migraine is an infrequent, tolerable inconvenience. For others, it is a devastating disorder resulting in frequent periods of incapacity, loss of productivity, and severely impaired quality of life.

Treatment

- Elimination of triggers
- For stress, behavioral interventions
- For mild headaches, acetaminophen or NSAIDs
- For severe attacks, triptans or dihydroergotamine plus a dopamine antagonist antiemetic

A thorough explanation of the disorder helps patients understand that although migraine cannot be cured, it can be controlled, enabling them to better participate in treatment.

Patients are urged to keep a written headache diary to document the number and timing of attacks, possible triggers, and response to treatment. Identified triggers are eliminated when possible. Patients should be encouraged to avoid triggers, and clinicians recommend behavioral interventions (biofeedback, stress management, psychotherapy) to manage migraine when stress is a major trigger or when analgesics are being overused.

Treatment of acute migraine headache is based on frequency, duration, and severity of attacks. It may include analgesics, antiemetics, triptans, and/or dihydroergotamine (1).

Mild to moderate attacks

NSAIDs or acetaminophen is used. Analgesics containing opioids, caffeine, or butalbital are helpful for infrequent, mild attacks but are prone to being overused, sometimes leading to a type of daily headache syndrome called medication overuse headache.

An antiemetic alone may be used to relieve mild or moderate attacks.

Severe attacks

If mild attacks evolve into incapacitating migraine or if attacks are severe from the onset, triptans are used. Triptans are selective serotonin 1B,1D receptor agonists. They are not analgesic per se but specifically block the release of vasoactive neuropeptides that trigger migraine pain. Triptans are most effective when taken at the onset of attacks. They are available in oral, intranasal, and sc forms (see Table: Drugs for Migraine and Cluster Headaches*); sc forms are more effective but have more adverse effects. Overuse of triptans can also lead to medication overuse headache. When nausea is prominent, combining a triptan with an antiemetic at the onset of attacks is effective.

IV fluids (eg, 1 to 2 L of 0.9% normal saline solution) can help relieve headache and increase a sense of well-being, especially in patients who are dehydrated from vomiting.

IV dihydroergotamine with a dopamine antagonist antiemetic (eg, metoclopramide 10 mg IV, prochlorperazine 5 to 10 mg IV) helps abort very severe, persistent attacks. Dihydroergotamine is also available in an sc form and as a nasal spray. A pulmonary-delivery formulation is being developed.

Triptans and dihydroergotamine can cause coronary artery constriction and are thus contraindicated in patients with coronary artery disease or uncontrolled hypertension; these drugs must be used with caution in elderly patients and in patients with vascular risk factors.

A good response to dihydroergotamine or a triptan should not be interpreted as diagnostic for migraine because these drugs may relieve headache due to subarachnoid hemorrhage and other structural abnormalities.

Prochlorperazine suppositories (25 mg) or tablets (10 mg) are an option for patients who cannot tolerate triptans and other vasoconstrictors.

Opioids should be used as a last resort (rescue drug) for severe headache when other measures are ineffective.

Chronic migraines

The same drugs used to prevent episodic migraine are used to treat chronic migraine. Also, supporting evidence is strong for onabotulinumtoxinA and, to a lesser extent, topiramate.

Drugs for Migraine and Cluster Headaches*

Drug	Dosage	Comments
Prevention		
Amitriptyline	10–100 mg po at bedtime	Used only for migraines

Treatment reference

1. Marmura MJ, Silberstein SD, Schwedt TJ : The acute treatment of migraine in adults: The American Headache Society evidence assessment of migraine pharmacotherapies. Headache 55(1):3–20, 2015.

Prevention

Daily preventive therapy is warranted when frequent migraines interfere with activity despite acute treatment. Some experts consider onabotulinumtoxinA the drug of choice.

For patients who use analgesics frequently (eg, > 2 days/wk), particularly those with medication overuse headache, preventive drugs (see Table: Drugs for Migraine and Cluster Headaches*) should be combined with a program for stopping overused analgesics. Choice of drug can be guided by coexisting disorders, as for the following:

- A small bedtime dose of amitriptyline for patients with insomnia

- A beta-blocker for patients with anxiety or coronary artery disease
- Topiramate, which can induce weight loss, for obese patients or for patients who wish to avoid weight gain
- Divalproex for patients with mania

Key Points

- Migraine is a common primary headache disorder with multiple potential triggers.
- Symptoms can include throbbing unilateral or bilateral pain, nausea, sensitivity to sensory stimuli (eg, light, sounds, smells), nonspecific prodromal symptoms, and temporary neurologic symptoms that precede headache (auras).
- Diagnose migraine based on clinical findings; if patients have red flag findings, tests are often needed.
- Involve patients in their care, including avoiding triggers and using biofeedback, stress management, and psychotherapy as appropriate.
- Treat most headaches with analgesics, IV dihydroergotamine, or triptans.
- If attacks are frequent and interfere with activities, use preventive therapy (eg, onabotulinumtoxinA, amitriptyline, a beta-blocker, topiramate, divalproex).

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Resources In This Article

Table 1 Drugs for Migraine and Cluster Headaches*

Drugs Mentioned In This Article

Drug Name	Select Trade
amitriptyline	No US brand name
topiramate	TOPAMAX
dihydroergotamine	D.H.E. 45, MIGRANAL
acetaminophen	TYLENOL
metoclopramide	REGLAN
prochlorperazine	COMPRO
Sumatriptan	IMITREX
Nadolol	CORGARD
Rizatriptan	MAXALT
Zolmitriptan	ZOMIG
Atenolol	TENORMIN
Lithium	LITHOBID
Eletriptan	RELPAX
Metoprolol	LOPRESSOR, TOPROL-XL
Almotriptan	AXERT
Naratriptan	AMERGE
Frovatriptan	FROVA
Propranolol	INDERAL
Verapamil	CALAN
Timolol	TIMOPTIC

Post–Lumbar Puncture and Other

Idiopathic Intracranial Hypertension

Yes No

Low–Pressure Headaches