Chapter 55: Headache: Migraine and Tension-Type

MIGRAINE HEADACHE

- *Migraine*, a common, recurrent, primary headache of moderate-to-severe intensity, interferes with normal functioning and is associated with gastrointestinal (GI), neurologic, and autonomic symptoms. In migraine with aura, focal neurologic symptoms precede or accompany the attack.

Pathophysiology

- Activation of trigeminal sensory nerves triggers the release of vasoactive neuropeptides, including calcitonin gene-related peptide (CGRP), neurokinin A, and substance P from perivascular axons. Vasodilation of dural blood vessels may occur with extravasation of dural plasma resulting in inflammation.
- Twin studies suggest 50% heritability of migraine, with a multifactorial polygenic basis. Migraine triggers may be modulators of the genetic set point that predisposes to migraine headache.
- Specific populations of serotonin (5-HT) receptors appear to be involved in the pathophysiology and treatment of migraine headache.

Clinical Presentation

- Migraine headache is characterized by recurring episodes of throbbing head pain, frequently unilateral.
- Up to 79% of patients with migraines have premonitory symptoms (not to be confused with aura) in the hours or days before headache onset. Neurologic symptoms (phonophobia, photophobia, hyperosmia, and difficulty concentrating) are most common, but psychological (anxiety, depression, euphoria, irritability, drowsiness, hyperactivity, and restlessness), autonomic (eg, polyuria, diarrhea, and constipation), and constitutional (eg, stiff neck, yawning, thirst, food cravings, and anorexia) symptoms may also occur.
- A migraine aura is experienced by approximately 25% of patients with migraines. Aura evolves over 5–20 minutes and lasts less than 60 minutes. Headache usually occurs within 60 minutes of the end of the aura. Visual auras can include both positive features (eg, scintillations, photopsia, teichopsia, and fortification spectrum) and negative features (eg, scotoma and hemianopsia). Sensory symptoms such as paresthesias or numbness of the arms and face, dysphasia or aphasia, weakness, and hemiparesis may also occur.
- Migraine headache may occur at any time but usually occurs in the early morning. Pain is usually gradual in onset, peaking in intensity over minutes to hours and lasting 4–72 hours. Pain is typically in the frontotemporal region and is moderate to severe. Headache is usually unilateral and throbbing with GI symptoms (eg, nausea and vomiting) almost invariably accompanying the headache. Other systemic symptoms include anorexia, constipation, diarrhea, abdominal cramps, nasal stuffiness, blurred vision, diaphoresis, facial pallor, and localized facial, scalp, or periorbital edema. Sensory hyperacuity (photophobia, phonophobia, or osmophobia) is frequent. Many patients seek a dark, quiet place.
- Once the headache pain wanes, a resolution phase characterized by exhaustion, malaise, and irritability ensues.

Diagnosis

- The International Headache Society (IHS) has published diagnostic criteria for classic migraine variants and other migraine subtypes
- A comprehensive headache history is essential and includes age at onset; frequency, timing, and duration of attacks; possible triggers; ameliorating factors; description and characteristics of symptoms; associated signs and symptoms; treatment history; and family and social history.

- Neuroimaging should be considered in patients with unexplained abnormal neurologic examination or atypical headache history.
- Onset of migraine headaches after age 50 suggests an organic etiology, such as a mass lesion, cerebrovascular disease, or temporal arteritis.

Treatment

- Goals of Treatment: The goal is to achieve consistent, rapid headache relief with minimal adverse effects and symptom recurrence, and minimal disability and emotional distress, enabling the patient to resume normal activities. Ideally, patients should be able to manage their headaches without emergency department or physician office visits.

Nonpharmacologic Treatment

- Apply ice to the head and recommend periods of rest or sleep, usually in a dark, quiet environment.
- Identify and avoid triggers of migraine attacks (**Table 55-1**).
- Behavioral interventions (relaxation therapy, biofeedback, and cognitive therapy) may help patients who prefer nondrug therapy or when drug therapy is ineffective or not tolerated.

TABLE 55-1

Commonly Reported Triggers of Migraine

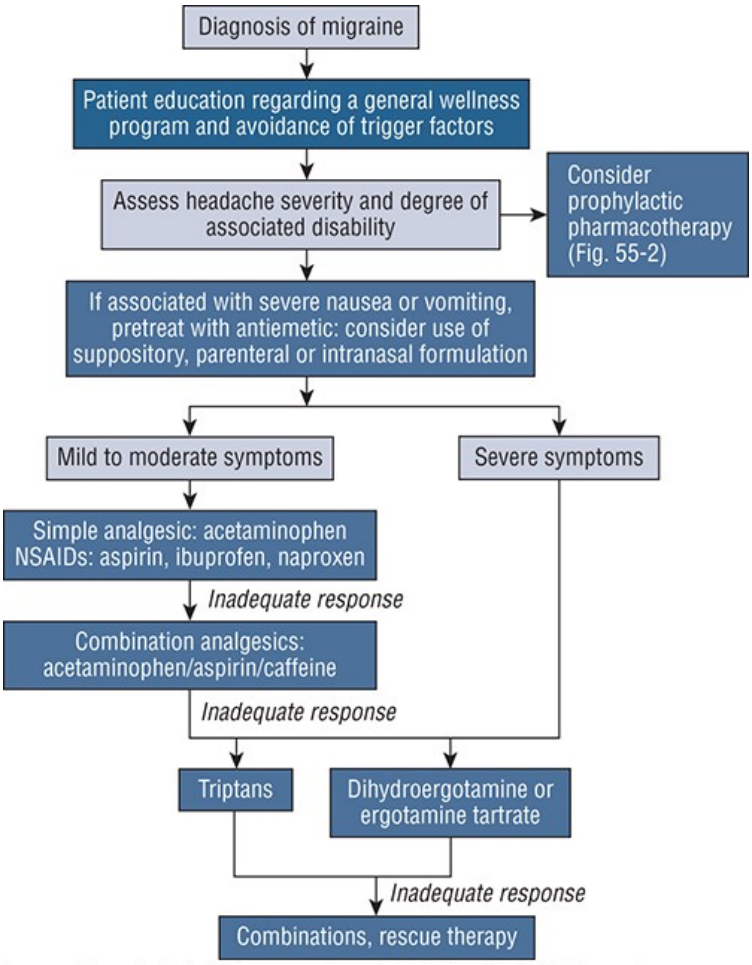
Food triggers	
Alcohol	
Caffeine/Caffeine withdrawal	
Chocolate	
Fermented and pickled foods	
Monosodium glutamate (eg, in Chinese food, seasoned salt, and instant foods)	
Nitrate-containing foods (eg, processed meats)	
Saccharin/Aspartame (eg, diet foods or diet sodas)	
Tyramine-containing foods	
Environmental triggers	**Behavioral–physiologic triggers**
Glare or flickering lights High altitude Loud noises Strong smells and fumes Tobacco smoke Weather changes	Excess or insufficient sleep Fatigue Menstruation, menopause Sexual activity Skipped meals Strenuous physical activity (eg, prolonged overexertion) Stress or poststress

Pharmacologic Treatment

- Administer acute migraine therapies at the onset of migraine (**Table 55-2** and **Figure 55-1**).

FIGURE 55-1

Treatment algorithm for migraine headaches.



Source: Terry L. Schwinghammer, Joseph T. DiPiro, Vicki L. Ellingrod, Cecily V. DiPiro: *Pharmacotherapy Handbook, 11e*

TABLE 55-2

Dosing of Acute Migraine Therapies[a]

Drug	Dose	Usual Range/Comments
Analgesics		
Acetaminophen[a] (Tylenol)	1000 mg at onset; repeat every 4–6 hours as needed	Maximum daily dose is 4 g
Acetaminophen 250 mg/aspirin 250 mg/caffeine 65 mg[a] (Excedrin Migraine)	2 tablets at onset and every 6 hours	Available over-the-counter as Excedrin Migraine

Nonsteroidal anti-inflammatory drugs		
Aspirin[a]	500–1000 mg every 4–6 hours	Maximum daily dose is 4 g
Ibuprofen[a] (Motrin)	200–800 mg every 6 hours	Avoid doses >2.4 g/day
Naproxen sodium[a] (Aleve, Anaprox)	550–825 mg at onset; can repeat 220 mg in 3–4 hours	Avoid doses >1.375 g/day
Diclofenac[a] (Cataflam, Voltaren)	50–100 mg at onset; can repeat 50 mg in 8 hours	Avoid doses >150 mg/day
Ergotamine tartrate		
Oral tablet (1 mg) with caffeine 100 mg[b] (Cafergot)	2 mg at onset; then 1–2 mg every 30 minutes as needed	Maximum dose is 6 mg/day or 10 mg/week; consider pretreatment with an antiemetic
Rectal suppository (2 mg) with caffeine 100 mg[b] (Cafergot, Migergot)	Insert 1/2–1 suppository at onset; repeat after 1 hour as needed	Maximum dose is 4 mg/day or 10 mg/week; consider pretreatment with an antiemetic
Dihydroergotamine		
Injection 1 mg/mL (D.H.E. 45)[b]	0.25–1 mg at onset IM, IV or subcutaneous; repeat every hour as needed	Maximum dose is 3 mg/day or 6 mg/week
Nasal spray 4 mg/mL[a] (Migranal)	One spray (0.5 mg) in each nostril at onset; repeat sequence 15 minutes later (total dose is 2 mg or 4 sprays)	Maximum dose is 3 mg/day; prime sprayer 4 times before using; do not tilt head back or inhale through nose while spraying; discard open ampules after 8 hours
Serotonin agonists (triptans)		
Sumatriptan[a] (Imitrex)	6 mg subcutaneous at onset; can repeat after 1 hour if needed	Maximum daily dose is 12 mg
Injection		
Oral tablets	25, 50, 85, or 100 mg at onset; can repeat after 2 hours if needed	Optimal dose is 50–100 mg; maximum daily dose is 200 mg; combination product with naproxen, 85/500 mg
Nasal spray	5, 10, or 20 mg at onset; can repeat after 2 hours if needed	Optimal dose is 20 mg; maximum daily dose is 40 mg; single-dose device delivering 5 or 20 mg; administer one spray in one nostril
Zolmitriptan[a] (Zomig, Zomig-ZMT)		
Oral tablets	2.5 or 5 mg at onset as regular or orally disintegrating tablet; can repeat after 2 hours if needed	Optimal dose is 2.5 mg; maximum dose is 10 mg/day

		Do not divide ODT dosage form
Nasal spray	5 mg (one spray) at onset; can repeat after 2 hours if needed	Maximum daily dose is 10 mg/day
Naratriptan[a] (Amerge)	1 or 2.5 mg at onset; can repeat after 4 hours if needed	Optimal dose is 2.5 mg; maximum daily dose is 5 mg
Rizatriptan[a] (Maxalt, Maxalt-MLT)	5 or 10 mg at onset as regular or orally disintegrating tablet; can repeat after 2 hours if needed	Optimal dose is 10 mg; maximum daily dose is 30 mg; onset of effect is similar with standard and orally disintegrating tablets; use 5-mg dose (15 mg/day maximum) in patients receiving propranolol
Almotriptan[a] (Axert)	6.25 or 12.5 mg at onset; can repeat after 2 hours if needed	Optimal dose is 12.5 mg; maximum daily dose is 25 mg
Frovatriptan[a] (Frova)	2.5 or 5 mg at onset; can repeat in 2 hours if needed	Optimal dose 2.5–5 mg; maximum daily dose is 7.5 mg (3 tablets)
Eletriptan[a] (Relpax)	20 or 40 mg at onset; can repeat after 2 hours if needed	Maximum single dose is 40 mg; maximum daily dose is 80 mg
Miscellaneous		
Metoclopramide[b] (Reglan)	10 mg IV at onset	Useful for acute relief in the office or emergency department setting
Prochlorperazine[b] (Compazine)	10 mg IV or IM, 25 mg rectally at onset	Useful for acute relief in the office or emergency department setting

[a]Limit use of symptomatic medications to fewer than 10 days/month when possible to avoid medication-overuse headache. Level A—established efficacy (≥2 Class I studies).

[b]Level B—probably effective (1 Class I or 2 Class II studies).

ODT, orally disintegrating tablet.

Antiemetic Pretreatment

- Pretreatment with an antiemetic (eg, **metoclopramide**, **chlorpromazine**, or **prochlorperazine**) 15–30 minutes before oral or nonoral migraine treatments (rectal suppositories, nasal spray, or injections) may be advisable when nausea and vomiting are severe. In addition to its antiemetic effects, metoclopramide helps reverse gastroparesis and enhances absorption of oral medications.
- **Prochlorperazine** (IM, IV, or rectal), **metoclopramide** (IV), as well as parenteral chlorpromazine and **droperidol** have been used for refractory migraine.
- Frequent or excessive use of acute migraine medications can result in increasing headache frequency and drug consumption known as medication-overuse headache. This occurs commonly with overuse of simple or combination analgesics, **opioids** **ergotamine tartrate**, and **triptans**. Limit use of acute migraine therapies to 2 or 3 days per week or 10 days per month.

Analgesics and Nonsteroidal Anti-Inflammatory Drugs

- Simple analgesics and nonsteroidal anti-inflammatory drugs (NSAIDs) are first-line treatments for mild to moderate migraine attacks; some

severe attacks are also responsive. **Aspirin**, **diclofenac**, **ibuprofen**, **naproxen sodium**, and the combination of **acetaminophen plus aspirin and caffeine** are effective. Evidence is limited with **ketorolac** and **flurbiprofen**.

- NSAIDs appear to prevent neurogenically mediated inflammation in the trigeminovascular system by inhibiting prostaglandin synthesis.
- Rectal analgesic preparations are options for patients with severe nausea and vomiting.
- The combination of acetaminophen, aspirin, and caffeine is approved in the United States for relieving migraine pain.
- Aspirin and acetaminophen are also available by prescription in combination with a short-acting barbiturate (**butalbital**). Use of these analgesics or narcotics should be limited because of concerns about overuse, medication-overuse headache, and withdrawal

Ergot Alkaloids and Derivatives

- Ergot alkaloids are useful for moderate to severe migraine attacks. They are non-selective $5HT_1$ receptor agonists that constrict intracranial blood vessels and inhibit the development of neurogenic inflammation in the trigeminovascular system. Venous and arterial constriction occurs.
- **Ergotamine tartrate** is available for oral, sublingual, and rectal administration. Oral and rectal preparations contain caffeine to enhance absorption and potentiate analgesia.
- **Dihydroergotamine (DHE)** is available for intranasal and parenteral (IM, IV, or subcutaneous [SC]) administration. Patients can self-administer IM or SC DHE. The nasal spray formulation of DHE has been shown to be effective.
- Nausea and vomiting are common with ergotamine derivatives, so consider antiemetic pretreatment and titrate to a dose that is not nauseating. Other common side effects include abdominal pain, weakness, fatigue, paresthesias, muscle pain, diarrhea, and chest tightness. Symptoms of severe peripheral ischemia (ergotism) include cold, numb, painful extremities; continuous paresthesias; diminished peripheral pulses; and claudication. Gangrenous extremities, myocardial infarction (MI), hepatic necrosis, and bowel and brain ischemia have occurred rarely with ergotamine. Do not use ergotamine derivatives and triptans within 24 hours of each other.
- Contraindications to use of ergot derivatives include renal and hepatic failure; coronary, cerebral, or peripheral vascular disease; uncontrolled hypertension; sepsis; and women who are pregnant or nursing.
- DHE does not appear to cause rebound headache, but dosage restrictions for ergotamine tartrate should be strictly observed to prevent this complication.

Serotonin Receptor Agonists (Triptans)

- The triptans (**Table 55-3**) are appropriate first-line therapies for patients with mild-to-severe migraine or as rescue therapy when nonspecific medications are ineffective.
- They are selective agonists of the $5HT_{1B}$ and $5HT_{1D}$ receptors. Relief of migraine headache results from: (1) normalization of dilated intracranial arteries, (2) inhibition of vasoactive peptide release, and (3) inhibition of transmission through second-order neurons ascending to the thalamus.
- **Sumatriptan** SC injection is packaged as an autoinjector device for self-administration. Compared with the oral formulation, SC administration offers enhanced efficacy and more rapid onset of action. Intranasal sumatriptan also has a faster onset of effect than the oral formulation and produces similar rates of response.
- Second-generation triptans (all except sumatriptan) have higher oral bioavailability and longer half-lives than oral sumatriptan, which could theoretically reduce headache recurrence. However, comparative clinical trials are necessary to determine their relative efficacy. **Frovatriptan** and **naratriptan** have the longest half-lives, slowest onset of action, and less headache recurrence.
- Pharmacokinetic characteristics of the triptans are shown in **Table 55-3**.
- Lack of response to one triptan does not preclude effective therapy with another triptan.

- Side effects of triptans include paresthesias, fatigue, dizziness, flushing, warm sensations, and somnolence. Minor injection site reactions are reported with SC use, and taste perversion and nasal discomfort may occur with intranasal administration.
- Up to 25% of patients report chest tightness; pressure; heaviness; or pain in the chest, neck, or throat. The mechanism of these symptoms is unknown, but a cardiac source is unlikely in most patients. Isolated cases of MI and coronary vasospasm with ischemia have been reported. Use triptans cautiously in patients at risk for unrecognized coronary artery disease. Do a cardiovascular assessment before giving triptans to postmenopausal women, men over 40 years of age, and patients with uncontrolled risk factors, and administer the first dose under medical supervision. Ischemic heart disease, uncontrolled hypertension, cerebrovascular disease, hemiplegic and basilar migraine, and pregnancy are contraindications to their use.
- Do not give triptans within 24 hours of ergotamine derivative administration or within 2 weeks of therapy with monoamine oxidase inhibitors. Concomitant use of triptans with selective serotonin reuptake inhibitors or serotonin–norepinephrine reuptake inhibitors can cause serotonin syndrome, a potentially life-threatening condition.

TABLE 55-3

Pharmacokinetic Characteristics of Triptans

Drug	Half-Life (Hours)	Time to Maximal Concentration (t_{max})	Bioavailability (%)	Elimination
Almotriptan	3–4	1.4–3.8 hours	80	MAO-A, CYP3A4, CYP2D6
Eletriptan	4–5	1–2 hours	50	CYP3A4
Frovatriptan	25	2–4 hours	24–30	Mostly unchanged, CYP1A2
Naratriptan	5–6	2–3 hours	63–74	Largely unchanged, CYP450 (various isoenzymes)
Rizatriptan	2–3		45	MAO-A
Oral tablets		1–1.2 hours		
Disintegrating		1.6–2.5 hours		
Sumatriptan	2			MAO-A
SC injection		12–15 minutes	97	
Oral tablets		2.5 hours	14	
Nasal spray		1–2.5 hours	17	
Zolmitriptan	3		40–48	CYP1A2, MAO-A
Oral		2 hours		
Disintegrating		3.3 hours		
Nasal		4 hours		

CYP, cytochrome P450; MAO-A, monoamine oxidase type A.

Opioids

- There is inadequate evidence for opioids and derivatives (eg, **meperidine**, **butorphanol**, **oxycodone**, and **hydromorphone**) for the treatment of migraines. Combinations of either oral **codeine** or **tramadol** and acetaminophen are probably effective, and **butorphanol** nasal spray has established efficacy.
- Reserve these for patients with moderate to severe infrequent headaches in whom conventional therapies are contraindicated or as rescue medication after failure to respond to conventional therapies. Closely supervise opioid therapy.

Prophylactic Therapy

- Prophylactic therapies (**Table 55-4** and **Figure 55-2**) are administered daily to reduce the frequency, severity, and duration of attacks, and to increase responsiveness to acute therapies.
- Consider prophylaxis in the setting of recurring migraines that produce significant disability; frequent attacks requiring symptomatic medication more than twice per week; symptomatic therapies that are ineffective, contraindicated, or produce serious side effects; uncommon migraine variants that cause profound disruption or risk of neurologic injury; and patient preference to limit the number of attacks.
- Preventive therapy may also be given intermittently when headaches recur in a predictable pattern (eg, exercise-induced or menstrual migraine).
- Because efficacy of various prophylactic agents appears to be similar, drug selection is based on side-effect profiles and comorbid conditions. Response to an agent is unpredictable, and a 2- to 3-month trial is necessary to achieve clinical benefit.
- Only **propranolol**, **timolol**, **divalproex sodium**, **topiramate**, **erenumab-aooe**, **fremanezumab-vfrm**, and **galcanezumab-gnlm** are Food and Drug Administration (FDA) approved for migraine prevention. Other established agents also have probable efficacy.
- Initiate prophylaxis with low doses, and advance slowly until a therapeutic effect is achieved or side effects become intolerable. Continue prophylaxis for at least 6–12 months after headache frequency and severity have diminished, and then gradual tapering or discontinuation may be reasonable.

FIGURE 55-2

Treatment algorithm for prophylactic management of migraine headaches.

(NSAID, nonsteroidal anti-inflammatory drug.)

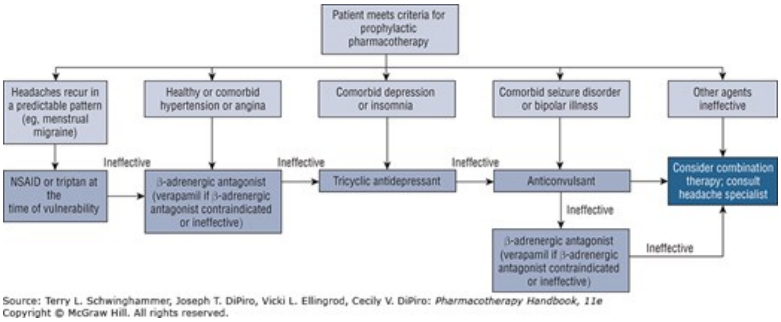


TABLE 55-4

Dosing of Prophylactic Migraine Therapies

Drug	Initial Dose	Usual Range	Comments
β-Adrenergic antagonists			
Atenolol[a] (Tenormin)	50 mg/day	50–200 mg/day	
Metoprolol[b] (Toprol, Toprol XL)	100 mg/day in divided doses	100–200 mg/day in divided doses	Dose short-acting 4 times a day and long-acting 2 times a day; available as extended release
Nadolol[a] (Corgard)	40–80 mg/day	80–240 mg/day	
Propranolol[b] (Inderal, Inderal LA)	40 mg/day in divided doses	40–160 mg/day in divided doses	Dose short-acting 2–3 times a day and long-acting 1–2 times a day; available as extended release

Timolol[b] (Blocadren)	20 mg/day in divided doses	20–60 mg/day in divided doses	
Antidepressants			
Amitriptyline[a] (Elavil)	10 mg at bedtime	20–50 mg at bedtime	
Venlafaxine[a] (Effexor, Effexor-XR)	37.5 mg/day	75–150 mg/day	Available as extended release; increase dose after 1 week
Anticonvulsants			
Topiramate[b] (Topamax)	25 mg/day	50–200 mg/day in divided doses	As effective as amitriptyline, propranolol, or valproate; increase by 25 mg/week
Valproic acid/Divalproex sodium[b] (Depakene, Depakote, Depakote ER)	250–500 mg/day in divided doses, or daily for extended release	500–1500 mg/day in divided doses, or daily for extended release	Monitor levels if compliance is an issue
Nonsteroidal anti-inflammatory drugs			
Ibuprofen[a] (Motrin)	400–1200 mg/day in divided doses	Same as initial dose	Use intermittently, such as for menstrual migraine prevention; daily or prolonged use may lead to medication-overuse headache and is limited by potential toxicity
Ketoprofen[a] (Orudis)	150 mg/day in divided doses	Same as initial dose	
Naproxen sodium[a] (Aleve, Anaprox)	550–1100 mg/day in divided doses	Same as initial dose	
Serotonin agonists (triptans)			
Frovatriptan[b] (Frova)	2.5 mg/day or 5 mg/day in divided doses	Same as initial dose	Taken in the perimenstrual period to prevent menstrual migraine
Naratriptan[a] (Amerge)	2 mg/day in divided doses	Same as initial dose	
Zolmitriptan[a] (Zomig)	5–7.5 mg/day in divided doses	Same as initial dose	
Miscellaneous			
Magnesium[a]	400 mg/day	800 mg/day in divided doses	May be more helpful in migraine with aura and menstrual migraine
MIG-99[a] (feverfew)	10–100 mg/day in divided doses	Same as initial dose	Withdrawal may be associated with increased headaches
Petasites[b]	100–150 mg/day in	150 mg/day in divided	Use only commercial preparations, plant is carcinogenic

	divided doses	doses	
Riboflavin[a]	400 mg/day in divided doses	400 mg/day in divided doses	Benefit only after 3 months

[a]Level B—probably effective (1 Class I or 2 Class II studies).

[b]Level A—established efficacy (≥2 Class I studies).

B-Adrenergic Antagonists

- **Propranolol**, **timolol**, and **metoprolol** reduce the frequency of migraine attacks by 50% in more than 50% of patients. **Atenolol** and **nadolol** are probably also effective.
- Side effects include drowsiness, fatigue, sleep disturbances, vivid dreams, memory disturbance, depression, sexual dysfunction, bradycardia, and hypotension.
- Use with caution in patients with heart failure, peripheral vascular disease, atrioventricular conduction disturbances, asthma, depression, and diabetes.

Antidepressants

- The tricyclic antidepressants (TCAs) **amitriptyline** and **venlafaxine** are probably effective for migraine prophylaxis. There are insufficient data to support or refute the efficacy of other antidepressants.
- Their beneficial effects in migraine prophylaxis are independent of antidepressant activity and may be related to downregulation of central $5HT_2$ receptors, increased synaptic norepinephrine, and enhanced opioid receptor actions.
- TCAs are usually well tolerated at the doses used for migraine prophylaxis, but anticholinergic effects may limit use, especially in elderly patients or those with benign prostatic hyperplasia or glaucoma. Evening doses are preferred because of sedation. Increased appetite and weight gain can occur. Orthostatic hypotension and slowed atrioventricular conduction are occasionally reported.

Anticonvulsants

- **Valproic acid**, **divalproex sodium** (a 1:1 molar combination of valproate sodium and valproic acid), and **topiramate** can reduce the frequency, severity, and duration of headaches. **Carbamazepine** is possibly effective.
- Side effects of valproic acid and divalproex sodium include nausea (less common with divalproex sodium and gradual dosing titration), tremor, somnolence, weight gain, hair loss, and hepatotoxicity (the risk of hepatotoxicity appears to be low in patients older than 10 years on monotherapy). Obtain baseline liver function tests. The extended-release formulation of divalproex sodium is administered once daily and is better tolerated than the enteric-coated formulation. Valproate is contraindicated in pregnancy and patients with a history of pancreatitis or chronic liver disease.
- Paresthesias (~50% of patients) and weight loss (9%–12% of patients) are common side effects of topiramate. Other side effects include fatigue, anorexia, diarrhea, difficulty with memory, language problems, taste perversions, and nausea. Use topiramate cautiously or avoid in those with a history of kidney stones or cognitive impairment.

Nonsteroidal Anti-Inflammatory Drugs

- NSAIDs are modestly effective for reducing the frequency, severity, and duration of migraine attacks. For migraine prevention, evidence for efficacy is strongest for naproxen and weakest for aspirin.

- They may be used intermittently to prevent headaches that recur in a predictable pattern (eg, menstrual migraine). Initiate up to 1 week before the time of headache vulnerability, and continue until vulnerability is passed.
- Potential GI and renal toxicity limit daily or prolonged use.

Calcitonin Gene-Related Peptide Antagonists

- Several anti-CGRP receptor monoclonal antibodies (**erenumab-aooe, fremanezumab-vfrm**, and **galcanezumab-gnlm**) have demonstrated efficacy in the prevention of episodic and chronic migraines (with or without aura). Concerns regarding their adverse effects were not substantiated in clinical trials. Data regarding long-term safety and efficacy are still needed. Cost and access may limit their use.

Other Drugs

- **Verapamil** has been widely used, but evidence for efficacy is inadequate.
- **Frovatriptan** is effective for prophylaxis of menstrual migraine, and **naratriptan** and **zolmitriptan** are probably effective.
- Other medications that may be effective include petasites, riboflavin (vitamin B_2), extract of feverfew, magnesium, subcutaneous histamine, lisinopril, candesartan, clonidine, guanfacine, and coenzyme Q10, but additional research is needed to confirm efficacy.

Evaluation of Therapeutic Outcomes

- Monitor patients taking abortive therapy for frequency of use of prescription and nonprescription medications and for side effects.
- Document patterns of abortive medication used to establish the need for prophylactic therapy. Monitor prophylactic therapies closely for adverse reactions, abortive therapy needs, adequate dosing, and compliance.

TENSION-TYPE HEADACHE

- *Tension-type headache*, the most common type of primary headaches, is more common in women than men. Pain is usually mild to moderate and nonpulsatile. Episodic headaches may become chronic in some patients.

Pathophysiology

- Pain is thought to originate from myofascial factors and peripheral sensitization of nociceptors. Central mechanisms are also involved. Mental stress, nonphysiologic motor stress, a local myofascial release of irritants, or a combination of these may be the initiating stimulus.

Clinical Presentation

- Premonitory symptoms and aura are absent, and pain is usually mild to moderate, bilateral (having a hatband pattern), and nonpulsatile.
- Mild photophobia or phonophobia may occur. Pericranial or cervical muscles may have tender spots or localized nodules in some patients.

Diagnosis

- The IHS has published diagnostic criteria for primary headache disorder.
- A comprehensive headache history is essential and includes age at onset; frequency, timing, and duration of attacks; possible triggers; ameliorating factors; description and characteristics of symptoms; associated signs and symptoms; treatment history; and family and social history.

Treatment

- Goals of Treatment: Pain relief and prevention of further headaches are the main desired outcomes of treatment.

Nonpharmacologic Therapy

- Nonpharmacologic therapies include reassurance and counseling, stress management, relaxation training, and biofeedback. Evidence supporting physical therapeutic options (eg, heat or cold packs, ultrasound, electrical nerve stimulation, massage, acupuncture, trigger point injections, and occipital nerve blocks) has been inconsistent.

Pharmacologic Therapy

Acute Treatment

- Simple analgesics (alone or in combination with caffeine) and NSAIDs are the mainstay of acute therapy. **Acetaminophen**, **aspirin**, **diclofenac**, **ibuprofen**, **naproxen**, **ketoprofen**, and **ketorolac** are effective.
- The combination of aspirin or acetaminophen with **butalbital**, or rarely, **codeine** are effective options, but avoid the use of butalbital and codeine combinations when possible. There is no evidence to support the efficacy of muscle relaxants.
- Give acute medication for episodic headache no more often than 3 days (butalbital-containing), 9 days (combination analgesics), or 15 days (NSAIDs) per month to prevent the development of chronic tension-type headache.

Prophylactic Therapy

- Consider preventive treatment if headache frequency is more than two per week, duration is longer than 3–4 hours, or severity results in medication overuse or substantial disability.
- The TCAs are used most often for prophylaxis of tension headache, but **venlafaxine**, **mirtazapine**, **gabapentin**, **topiramate**, and **tizanidine** may also be effective. Limited data suggest that trigger point injections of lidocaine may reduce headache frequency.

Evaluation of Therapeutic Outcomes

- Monitor for frequency, intensity, and duration of headaches and for any change in the headache pattern. Encourage patients to keep a headache diary to document frequency, duration, and severity of headaches, headache response, and potential triggers of migraine headaches.

See Chapter 78, Headache Disorders, authored by T. Kristopher Harrell and Deborah S. Minor, for a more detailed discussion of this topic.