

**TABLE 111-6** PREVENTIVE THERAPIES FOR MIGRAINE

DRUG CLASS	AGENT	DOSE RANGE	EVIDENCE LEVEL	ADVERSE EFFECTS
β-adrenoceptor blockers	Propranolol	80-240 mg	A	Contraindicated in asthma, syncope
	Metoprolol	50-150 mg	A	
	Timolol	10-20 mg	A	
Antiepileptic drugs	Divalproex sodium	200-1500 mg	A	Weight gain, thrombocytopenia, tremor Renal calculi, weight loss, amnesia, glaucoma, dysequilibrium
	Topiramate	25-150 mg	A	
	Gabapentin	300-1800 mg	U	
Antidepressants	Amitriptyline	10-150 mg	B	Somnolence Insomnia, hypertension
	Nortriptyline	25-100 mg	N/A	
	Venlafaxine	37.5-150 mg	B	
Calcium channel blockers	Verapamil	180-480 mg	U	Constipation, hypotension, edema Weight gain, depression
	Flunarizine*	5-10 mg	N/A	
Other	Onabotulinum toxin A	Variable	N/A	Discomfort, ecchymosis

Level of Evidence A, Medication with established efficacy; Level B, medication probably effective; Level U, inadequate data to support use; N/A, not considered in recent evidence review.

\*Not available in the US.

release of CGRP; telcagepant, a CGRP receptor antagonist has been found to have similar efficacy to oral triptan therapy. Greater insights into the genetic basis for migraine has enhanced our understanding of ion channel dysfunction in this disorder, and are likely to lead to new therapeutic targets.

## Cluster Headache

### Clinical Features

Cluster headache is the prototypic trigeminal autonomic cephalgia, entirely distinct from migraine, although there may be some clinical overlap. It is uncommon, occurring in less than 10% of all patients with headache. Unlike migraine, it is much more common in men than in women, and the mean age at onset is later in life. Also, unlike migraine, cluster headache rarely begins in childhood, and there is less often a family history. The pain in cluster headache is of extreme intensity, is strictly unilateral, and is associated with congestion of the nasal mucosa and injection of the conjunctiva on the side of the pain. Increased sweating of the ipsilateral side of the forehead and face may occur. There may be associated ocular signs of Horner syndrome: miosis, ptosis, and the additional feature of eyelid edema. Attacks often awaken patients, usually 2 to 3 hours after the onset of sleep (“alarm-clock headache”). In contrast to migraineurs, the pain is not relieved by resting in a dark, quiet area; on the contrary, patients sometimes seek activity that can distract them. The duration of headache is usually around 1 hour, although it may recur several times in a day, paroxysmally (in *clusters*) for several weeks.

These periods of frequent headaches are separated by headache-free periods of varying duration, often several months or years. Attacks have a striking tendency to be precipitated by even small amounts of alcohol. There are rare variants of cluster headache: a “chronic variety” in which remissions are brief (less than 14 days); “*chronic paroxysmal hemicrania*,” in which attacks are shorter and strikingly more prevalent in women; and “*hemicrania continua*,” in which there is continuous, moderately severe, unilateral headache. The cause of all these syndromes is unknown, although the distribution of the pain suggests dysfunction of the trigeminal nerve.

### Treatment

Therapy for cluster headache may be abortive for acute headache or prophylactic to prevent headache. Acute headache may respond to oxygen by mask (7 to 10 L/min for 15

minutes), which is effective within several minutes in 70% of patients. Sumatriptan and dihydroergotamine are also effective. Preventive medications include lithium, divalproex sodium, verapamil, methysergide, and corticosteroids. Paroxysmal hemicrania and related syndromes are often strikingly responsive to indomethacin.

## Tension-Type Headache

In contrast to migraine, tension-type headache is featureless. The pain is usually not throbbing, but rather steady and often described as a “pressure feeling” or a “viselike” sensation. It is usually not unilateral and may be frontal, occipital, or generalized. There is frequently pain in the neck area, unlike in migraine. Pain commonly lasts for long periods of time (days) and does not rapidly appear and disappear in attacks. There is no “aura.” Photophobia and phonophobia are not prominent. Although tension-type headache may be related by the patient to occur or be exacerbated at times of particular emotional stress, the pathophysiology may relate to sustained craniocervical muscle contraction; hence, a more useful term for this syndrome is *muscle-contraction headache*.

A careful evaluation should be made of the patient’s psychosocial milieu and the presence of anxiety or depression. The tricyclic antidepressant drugs in low doses have proven the most useful for prevention of tension-type headache. Although the best documented is amitriptyline, newer agents with fewer side effects may be equally effective. Nonpharmacologic therapies such as relaxation therapy, massage, physiotherapy, or acupuncture may be useful in refractory cases. Intramuscular botulinum toxin injections have been used both in migraine and tension-type headache, but are of established benefit only in patients with chronic migraine.

## Other Defined Primary Headache Syndromes

Other acute short-lasting headache syndromes need to be differentiated from migraine, cluster, or tension headache. These include primary “thunderclap” headache, *primary stabbing headache*, *primary exertional headache*, and coital headache. The latter may be indistinguishable from the headache of intracranial aneurysm rupture and requires computed tomography (CT) and lumbar puncture to exclude subarachnoid hemorrhage (SAH). All of these headache syndromes are more common in migraineurs. Two additional rare, short-lasting headache