HEADACHE

Headache is among the most common reasons patients seek medical attention.

The International Classification of Headache Disorders (ICHD-2) divides headaches into

Primary headache :in which headache itself is the illness and no other etiology is diagnosed.(Migraine, tension-type headache, and cluster headache)

Secondary headache :Headache attributed to an identifiable structural or metabolic abnormality. (low-pressure headache and idiopathic intracranial hypertension)

Primary Headache		Secondary Headache	
Type	**%**	**Type**	**%**
Tension-type	69	Systemic infection	63
Migraine	16	Head injury	4
Idiopathic stabbing	2	Vascular disorders	1
Exertional	1	Subarachnoid hemorrhage	<1
Cluster	0.1	Brain tumor	0.1

Table 14-2 Headache Symptoms that Suggest a Serious Underlying Disorder
"Worst" headache ever
First severe headache
Subacute worsening over days or weeks
Abnormal neurologic examination
Fever or unexplained systemic signs
Vomiting that precedes headache
Pain induced by bending, lifting, cough
Pain that disturbs sleep or presents immediately upon awakening
Known systemic illness
Onset after age 55
Pain associated with local tenderness, e.g., region of temporal artery

Secondary Headache

management focuses on diagnosis and treatment of the underlying condition.

- **Meningitis**
- **Intracranial Hemorrhage**
- **Brain Tumor**

30% of patients with brain tumors presented with headache.

The head pain is usually an intermittent deep, dull aching of moderate intensity, which may worsen with exertion or change in position and may be associated with nausea and vomiting (same pattern ocuur in migraine patient).

- The headache of brain tumor disturbs sleep in about 10% of patients.
- Vomiting that precedes the appearance of headache by weeks is highly characteristic of posterior fossa brain tumors.
- A history of amenorrhea or galactorrhea (pituitary adenoma).
- Headache in a patient with known malignancy suggests either cerebral metastases or carcinomatous meningitis.
- Head pain appearing abruptly after bending, lifting, or coughing can be due to a posterior fossa mass, a Chiari malformation, or low CSF volume.

➢ Temporal (giant cell) Arteritis

- an inflammatory disorder of arteries that frequently involves the extracranial carotid circulation.

- It is common in elderly; the average age of onset is 70 years, and women account for 65% of cases.

- About half of patients with untreated temporal arteritis develop blindness due to involvement of the ophthalmic artery and its branches.

- Because treatment with glucocorticoids is effective in preventing this complication, prompt recognition of the disorder is important.

- Typical presenting symptoms include headache, polymyalgia rheumatica, jaw claudication, fever, and weight loss.
- Headache is the dominant symptom and may be unilateral or bilateral and is located temporally in 50% of patients.
- Pain usually described as dull and boring, and most patients can recognize that the origin of their head pain is superficial, rather than originating deep within the cranium (the pain site for migraineurs).
- Scalp tenderness is present, often to a marked degree; brushing the hair or resting the head on a pillow may be impossible because of pain.
- Headache is usually worse at night and often aggravated by exposure to cold.

- ESR is often, though not always, elevated; a normal ESR does not exclude giant cell arteritis.

- A temporal artery biopsy

immediate treatment with prednisone 80 mg daily for the first 4–6 weeks should be initiated when clinical suspicion is high.

Migraine Headache

Epidemiology

- About 18% of women, 6% of men, and 4% of children have migraine.

- The disorder usually begins in the first three decades of life, and prevalence peaks in the fifth decade. Attacks usually decrease in severity and frequency after age 40 years.

  Onset of migraine after age 50 years is rare.

Migraine and vascular disorders

Migraineurs (especially with aura), have increased risk of ischemic stroke (posterior circulation stroke) and cerebrovascullar disorders.

Pathogenesis

The brain of the migraineur is particularly sensitive to environmental and sensory stimuli. This sensitivity is probably due to dysfunction of monoaminergic sensory control systems located in the brainstem and thalamus.

A genetic component to migraine is indicated by the fact that approximately 70% of patients have a first-degree relative with a history of migraine.

In addition, a variety of environmental and behavioral factors may precipitate migraine attacks.

Migraine can often be recognized by its activators, referred to as *triggers.*

- Hormonal changes, such as those accompanying menstruation
- Stress
- Excessive or insufficient sleep
- Medications (eg, vasodilators, oral contraceptives)
- Smoking
- Exposure to bright or fluorescent lighting
- Strong odors (eg, perfumes, colognes, petroleum distillates)
- Head trauma
- Weather changes
- Motion sickness
- Cold stimulus (eg, ice cream headaches)
- Lack of exercise
- Fasting or skipping meals
- Red wine

Certain foods and food additives have been suggested as potential precipitants of migraine, including the following:

- Caffeine
- Artificial sweeteners (eg, aspartame, saccharin)
- Monosodium glutamate (MSG)
- Citrus fruits
- Foods containing tyramine (eg, aged cheese)
- Meats with nitrites

Clinical presentation

- Migraine attacks commonly occur when the migraineur is awake.
- headache usually throbbing or pulsatile, and initially is unilateral and localized in the frontotemporal and ocular area.
- Pain intensity is moderate to severe and intensifies with movement or physical activity.
- Many patients prefer to lie quietly in a dark room.
- The headache typically lasts from 4-72 hours, and subsides gradually after a period of sleep.

Diagnostic Criteria

patients must have had at least 5 headache attacks that lasted 4-72 hours.

and the headache must have had at least 2 of the following characteristics :

- Unilateral location
- Pulsating quality
- Moderate or severe pain intensity
- Aggravation by or causing avoidance of routine physical activity (eg, walking, climbing stairs)

In addition, during the headache the patient must have had at least 1 of the following:

- Nausea and/or vomiting
- Photophobia and phonophobia

International Headache Society
Criteria for Migraine Without Aura

5 or more episodic headaches lasting 4-72 hours with:

Any 2 of the following:

Unilateral location

Throbbing/pulsating

Worsened by movement

Moderate or severe intensity

+

Any 1 of the following:

Nausea or vomiting

Phonophobia/photophobia

Prodrome

About 60% of patients report premonitory symptoms that occur hours to days before headache onset, which include the following:

- Heightened sensitivity to light, sound, and odors
- Lethargy or uncontrollable yawning
- Food cravings
- Mental and mood changes (eg, depression, anger, euphoria)
- Excessive thirst and polyuria
- Fluid retention
- Anorexia
- Constipation or diarrhea

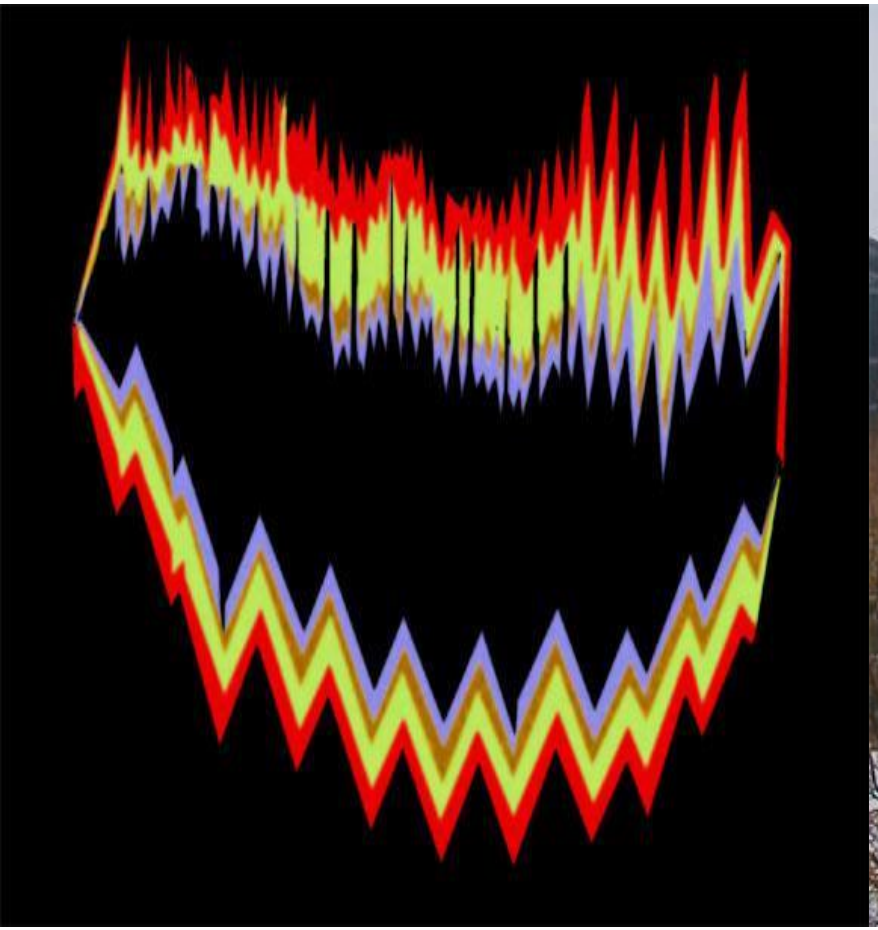
Aura

- May precede or accompany the headache phase or may occur in isolation

- Usually develops over 5-20 minutes and lasts less than 60 minutes
- Most commonly visual but can be sensory, motor, or any combination of these
- The most common visual phenomenon is the scintillating scotoma, an arc or band of absent vision with a shimmering or glittering zigzag border

- *Sensory symptoms*, Paresthesias, occurring in 40% of cases may be followed by numbness.

- *Motor symptoms* often are described as a sense of heaviness of the limbs, may associated with Speech and language disturbances.



Treatment

Reduction of Migraine Triggers

Patients should avoid factors that precipitate a migraine attack (eg, lack of sleep, fatigue, stress, certain foods, use of vasodilators).

Nonpharmacologic Therapy

Biofeedback, cognitive-behavioral therapy, and relaxation therapy are frequently effective against migraine.

FDA approved the Cerena Transcranial Magnetic Stimulator (Cerena TMS), the first device to relieve pain caused by migraine headache with aura for use in patients aged 18 years and older.

Acute Attack Therapies for Migraine

The choice for an individual patient depends on:

- the severity of the attacks.
- associated symptoms such as nausea and vomiting.
- comorbid problems.
- patient's treatment response.

Three major pharmacologic classes:

- anti-inflammatory agents.
- 5-$HT_{1B/1D}$ receptor agonists.
- dopamine receptor antagonists.

In general, an adequate dose of whichever agent is chosen should be used as soon as possible after the onset of an attack. If additional medication is required within 60 min because symptoms return or have not abated, the initial dose should be increased for subsequent attacks.

Nonsteroidal Anti-Inflammatory Drugs (NSAIDs)

- can reduce both the severity and duration of a migraine attack.
- their effectiveness in migraine is usually less than optimal in moderate or severe migraine attacks.
- The combination of acetaminophen, aspirin, and caffeine has been approved for use by the (FDA) for the treatment of mild to moderate migraine.
- The combination of aspirin and metoclopramide is comparable to a single dose of sumatriptan.

5-HT_1 Receptor Agonists

- Ergotamine and dihydroergotamine are nonselective receptor agonists.

- triptans are selective 5-$HT_{1B/1D}$ receptor agonists.
  (naratriptan, rizatriptan, eletriptan, sumatriptan, zolmitriptan, almotriptan, and frovatriptan).

- Rizatriptan and eletriptan are the most efficacious of the triptans.

- Sumatriptan and zolmitriptan have similar rates of efficacy as well as time to onset, with an advantage of having multiple formulations.

- whereas almotriptan, frovatriptan, and naratriptan are somewhat slower in onset and are better tolerated.

Disadvantages of triptans:

- monotherapy does not result in rapid, consistent, and complete relief of migraine in all patients.
- Triptans are not effective in migraine with aura unless given after the aura is completed and the headache initiated.
- Side effects are common though often mild and transient.
- are contraindicated in individuals with a history of cardiovascular and cerebrovascular disease.
- Recurrence of headache which occurs at least occasionally in most patients.

coadministration of a longer-acting NSAID, naproxen 500 mg, with sumatriptan (Treximet) will augment the initial effect of sumatriptan and, importantly, reduce rates of headache recurrence.

All the triptans are most effective when taken early during a migraine and all may be repeated in 2 hours as needed, with a maximum of 2 doses daily.

Triptans should not be used more than 3 days weekly, to avoid transformed migraine and medication overuse headach.

- oral formulations of ergotamine also contain 100 mg caffeine (enhance ergotamine absorption and possibly to add additional analgesic activity).

- The average oral ergotamine dose for a migraine attack is 2 mg.

- In general, ergotamine appears to have a much higher incidence of nausea than triptans, but less headache recurrence.

Do not administer vasoconstrictors, such as ergots or triptans, to patients with known complicated migraine

Nasal

dihydroergotamine (Migranal), zolmitriptan (Zomig nasal), or sumatriptan.

Although they provide faster and more effective relief of a migraine attack than oral formulations, their reported efficacy is only approximately 50–60%.

Parenteral

Parenteral administration of dihydroergotamine and sumatriptan is approved for the rapid relief of a migraine attack.

If an attack has not already peaked, SC or IM administration of 1 mg dihydroergotamine suffices for about 80–90% of patients. Sumatriptan, 6 mg SC, is effective in 70–80% of patients.

Dopamine Antagonists

Oral

Drug absorption is impaired during migraine (even in the absence of nausea) because of reduced gastrointestinal motility.

Therefore, when oral NSAIDs and/or triptan agents fail, the addition of a dopamine antagonist such as metoclopramide 10 mg should be considered to enhance gastric absorption.

Parenteral

Parenteral dopamine antagonists (e.g., chlorpromazine, prochlorperazine, metoclopramide) can also provide significant acute relief of migraine; they can be used in combination with parenteral 5-$HT_{1B/1D}$ agonists.

Preventive Treatments for Migraine

indications for prophylactic migraine therapy:

- Frequency of migraine attacks is greater than 2 per month
- Duration of individual attacks is longer than 24 hours
- The headaches cause major disruptions in the patient's lifestyle, with significant disability that lasts 3 or more days
- Symptomatic medications are contraindicated or ineffective
- Use of abortive medications more than twice a week
- Migraine variants such as hemiplegic migraine.

The goals of preventive therapy are as follows:

- Reduce attack frequency, severity, and/or duration
- Improve responsiveness to acute attacks
- Reduce disability

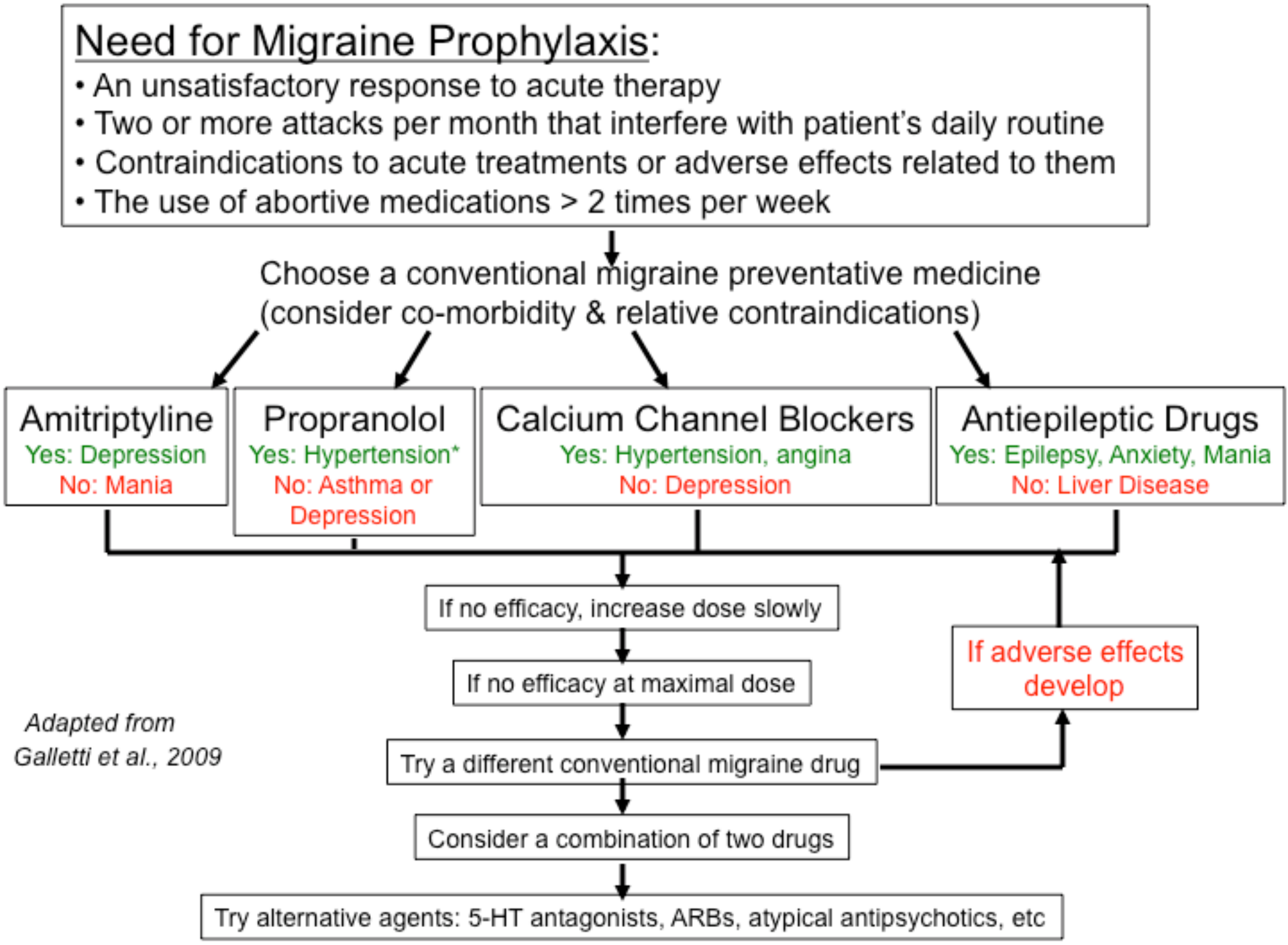
The major prophylactic medications for migraine work via one of the following mechanisms:

- 5-HT2 antagonism - Methysergide
- Regulation of voltage-gated ion channels - Calcium channel blockers
- Modulation of central neurotransmitters - Beta blockers, tricyclic antidepressants
- Enhancing gamma-aminobutyric acid-ergic (GABAergic) inhibition - Valproic acid, gabapentin

- As with abortive medications, the selection of a preventive medication must take into consideration comorbid conditions and the side-effect profile.

- Most preventive medications have modest efficacies and have therapeutic gains of less than 50% when compared with placebo.

- The latency between initiation of therapy and onset of positive treatment response can be quite prolonged.


Need for Migraine Prophylaxis:
• An unsatisfactory response to acute therapy
• Two or more attacks per month that interfere with patient's daily routine
• Contraindications to acute treatments or adverse effects related to them
• The use of abortive medications > 2 times per week
Choose a conventional migraine preventative medicine
(consider co-morbidity & relative contraindications)
Amitriptyline
Yes: Depression
No: Mania
Propranolol
Yes: Hypertension*
No: Asthma or Depression
Calcium Channel Blockers
Yes: Hypertension, angina
No: Depression
Antiepileptic Drugs
Yes: Epilepsy, Anxiety, Mania
No: Liver Disease
If no efficacy, increase dose slowly
If no efficacy at maximal dose
Try a different conventional migraine drug
Consider a combination of two drugs
Try alternative agents: 5-HT antagonists, ARBs, atypical antipsychotics, etc
If adverse effects develop
Adapted from
Galletti et al., 2009

Tension-type headache

Tension-type headache (TTH) is very common, with a lifetime prevalence of 69% in men and 88% in women.

It can begin at any age, but onset during adolescence or young adulthood is most common.

Clinical features

Episodic TTHs can be either infrequent (<1 day/month) or frequent (>1 but <15 days/month)

The ICHD-2 requires at least 10 previous headaches, each lasting 30 minutes to 7 days (median 12 hours), with at least two of the following characteristics:

- a pressing/tightening (non-pulsating) quality (band-like)
- mild to moderate intensity.
- bilateral location.
- no aggravation with physical activity.
- the patient should not have nausea or vomiting or a combination of photophobia and phonophobia.

Treatment

The pain of TTH can generally be managed with simple analgesics such as acetaminophen, aspirin, or NSAIDs.

Behavioral approaches including relaxation can also be effective.

Narcotics and combination analgesics that contain sedatives *should be limited,* because overuse may cause dependence.

Preventive therapy

should be administered when a patient has frequent headaches that produce disability or may lead to symptomatic medication overuse.

Medications used for prevention include:

- antidepressants.
- beta blockers.
- anticonvulsants.

Antidepressants are the medication *of first choice*. An adequate trial period of *at least 1–2 months* must be allowed.

Trigeminal Autonomic Cephalalgias (TACs)

Are group of primary headaches including

- cluster headache.
- paroxysmal hemicrania.
- SUNCT (*s*hort-lasting *u*nilateral *n*euralgiform headache attacks with *c*onjunctival injection and *t*earing)/SUNA (*s*hort-lasting *u*nilateral *n*euralgiform headache attacks with cranial *a*utonomic symptoms).

TACs are characterized by:

- short-lasting attacks of head pain
- cranial autonomic symptoms, such as lacrimation, conjunctival injection, or nasal congestion.
- Pain is usually severe and may occur more than once a day.

Cluster Headache

Cluster headache affects predominantly middle-aged men (men are affected three times more often than women).

Episodes of severe unilateral periorbital pain occur daily for several weeks and are often accompanied by one or more of the following:

- ipsilateral nasal congestion and rhinorrhea.
- lacrimation and redness of the eye.
- Horner syndrome.

During attacks, patients are often *restless and agitated* tend to move, pacing, rocking, or rubbing their head for relief.

This is in sharp contrast to patients with migraine, who prefer to remain *motionless* during attacks.

Episodes typically occur at night, awaken the patient, and last for between 15 minutes and 3 hours.

Spontaneous remission then occurs, and the patient remains well for weeks or months before another bout of closely spaced attacks.

Bouts may last for 4 to 8 weeks and may occur up to several times per year.

Alcohol, stress, glare, or ingestion of specific foods occasionally precipitates attacks.

Acute Attack Treatment

- Cluster headache attacks peak rapidly, and thus a treatment with quick onset is required.

- Many patients with acute cluster headache respond very well to oxygen inhalation. This should be given as 100% oxygen at 10–12 L/min for 15–20 min.

- Sumatriptan 6 mg SC is rapid in onset and will usually shorten an attack to 10–15 min. Sumatriptan (20 mg) and zolmitriptan (5 mg) nasal sprays are both effective.

Prevention

Short-term

- A 10-day course of prednisone, beginning at 60 mg daily for 7 days and followed by a rapid taper, may interrupt the pain bout for many patients.

- ergotamine (1–2 mg), is most effective when given 1–2 h before an expected attack.

Long-term

- verapamil is the first-line preventive treatment for patients with chronic cluster headache or prolonged bouts. The initial dose range is 40–80 mg twice daily; effective doses may be as high as 960 mg/d.

- Lithium (600–900 mg qd) appears to be particularly useful for the chronic form of the disorder.

When medical therapies fail in chronic cluster headache, neurostimulation strategies can be employed.

Table 14-9 Preventive Management of Cluster Headache	
Short-Term Prevention	**Long-Term Prevention**
Episodic Cluster Headache	**Episodic Cluster Headache & Prolonged Chronic Cluster Headache**
Prednisone 1 mg/kg up to 60 mg qd, tapering over 21 days	Verapamil 160–960 mg/d
	Lithium 400–800 mg/d
Methysergide 3–12 mg/d	Methysergide 3–12 mg/d
Verapamil 160–960 mg/d	Topiramate[a] 100–400 mg/d
Greater occipital nerve injection	Gabapentin[a] 1200–3600 mg/d
	Melatonin[a] 9–12 mg/d

Paroxysmal Hemicrania

The essential features of PH are:

- unilateral, very severe pain
- short-lasting attacks (2–45 min).
- very frequent attacks (usually more than five a day).
- marked autonomic features ipsilateral to the pain.
- rapid course (<72 h).
- excellent response to indomethacin (25-75mg).

In contrast to cluster headache, which predominantly affects males, the male:female ratio in PH is close to 1:1.

Secondary PH has been reported with lesions in the region of the *sella turcica.*

(arteriovenous malformation, cavernous sinus meningioma, and epidermoid tumors).

Secondary PH is more likely:

- if the patient requires high doses (>200 mg/d) of indomethacin.

- In patients with apparent bilateral PH.

When a diagnosis of PH is considered, MRI is indicated to exclude a pituitary lesion.

Sunct/Suna

SUNCT (*s*hort-lasting *u*nilateral *n*euralgiform headache attacks with *c*onjunctival injection and *t*earing)

is a rare primary headache syndrome characterized by severe, unilateral orbital or temporal pain that is stabbing or throbbing in quality.

Diagnosis requires at least 20 attacks, lasting for 5–240 s; ipsilateral conjunctival injection and lacrimation should be present.

In some patients conjunctival injection or lacrimation is missing, and the diagnosis of SUNA (*s*hort-lasting *u*nilateral *n*euralgiform headache attacks with cranial *a*utonomic symptoms) can be made.

SUNCT can be seen with posterior fossa or pituitary lesions.

All patients with SUNCT/SUNA should be evaluated with pituitary function tests and a brain MRI with pituitary views.

Abortive Therapy

Therapy of acute attacks is not a useful concept in SUNCT/SUNA since the attacks are of such short duration. However, IV lidocaine, which arrests the symptoms, can be used in hospitalized patients.

Preventive Therapy

Long-term prevention to minimize disability and hospitalization is the goal of treatment. The most effective treatment for prevention is lamotrigine, 200–400 mg/d. Topiramate and gabapentin may also be effective. Carbamazepine, 400–500 mg/d, has been reported by patients to offer modest benefit

Table 14-8 Clinical Features of the Trigeminal Autonomic Cephalalgias			
	Cluster Headache	**Paroxysmal Hemicrania**	**SUNCT**
Gender Pain	M > F	F = M	F ~ M
Type	Stabbing, boring	Throbbing, boring, stabbing	Burning, stabbing, sharp
Severity	Excruciating	Excruciating	Severe to excruciating
Site	Orbit, temple	Orbit, temple	Periorbital
Attack frequency	1/alternate day–8/d	1–40/d (>5/d for more than half the time)	3–200/d
Duration of attack	15–180 min	2–30 min	5–240 s
Autonomic features	Yes	Yes	Yes (prominent conjunctival injection and lacrimation)[a]
Migrainous features[b]	Yes	Yes	Yes
Alcohol trigger	Yes	No	No
Cutaneous triggers	No	No	Yes
Indomethacin effect	—	Yes[c]	—
Abortive treatment	Sumatriptan injection or nasal spray	No effective treatment	Lidocaine (IV)
	Oxygen		
Prophylactic treatment	Verapamil	Indomethacin	Lamotrigine Topiramate
	Methysergide		
	Lithium		Gabapentin