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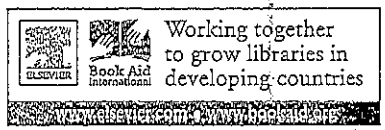

CHAPTER 21

HEADACHES

Randolph W. Evans

GENERAL PRINCIPLES

1. What is the prevalence of headaches?
Having had any type of headache is a near universal experience, with a lifetime prevalence of 90% and a 1-year prevalence of over 50% (migraine 12% and tension type 38%). Migraine is the third most prevalent disorder and seventh highest specific cause of disability worldwide. Approximately 90% of headaches in patients with a normal neurologic examination are primary (such as migraine, tension type, and cluster). The remaining 10% are due to numerous secondary causes. There are over 300 different types and causes of headaches. Since there are only so many ways your head can hurt, there is overlap between the symptoms of primary and secondary headaches, although different headache types may have signature features.

This chapter will often use definitions and present headaches in the order found in the *International Classification of Headache Disorders*, 3rd edition, beta version (ICHD-3), which is the international standard for classification and diagnosis of headache disorders.

2. Which cranial structures are sensitive to pain?
Although all pain is registered in the brain, the brain itself is not pain sensitive. The arachnoid, ependyma, and dura (except portions near blood vessels) are also insensitive to pain. The following are sensitive to pain: cranial nerves V, VII, IX, and X; the circle of Willis and proximal continuations; meningeal arteries; large veins in the brain and dura; and structures external to the skull (including scalp and neck muscles, cutaneous nerves and skin, the mucosa of paranasal sinuses, external auditory canal and tympanic membrane, orbital structures and eyeballs, salivary glands, teeth, temporomandibular joints, cervical nerves and roots, and the external carotid arteries and branches).

3. What are the key questions to ask for a headache history?
A detailed headache history is essential for establishing the diagnosis (Table 21-1).

4. What are the reasons to consider neuroimaging for headaches?
Most patients do not need neuroimaging. Again, 90% of patients have primary headaches with a diagnosis made by a detailed history and normal neurologic examination.

Neuroimaging should be considered for those patients whose temporal and headaches features include the following: (1) the "first or worst" headache; (2) subacute headaches with increasing frequency or severity; (3) a progressive or new daily persistent headache; (4) chronic daily headache; (5) headaches always on the same side; (6) headaches not responding to treatment; and (7) headaches triggered by cough, exertion, or Valsalva manuever. Patient demographics and comorbidities that should prompt consideration of neuroimaging include headaches cooccurring with seizures, a history of cancer or immunosuppression (human immunodeficiency virus [HIV]-infected or iatrogenically immunosuppressed), pregnancy or the postpartum period, and new-onset headache in those over 50 years of age. Worrisome associated symptoms and signs prompting neuroimaging include headaches associated with fever, stiff neck, nausea, and vomiting, headaches other than migraine with aura associated with focal neurologic symptoms or signs, and headaches associated with papilledema, cognitive impairment, or personality change. The likelihood that either computed tomography (CT) or magnetic resonance imaging (MRI) will reveal an abnormality responsible for the headache in patients with any headache and a normal neurologic examination is approximately 2%. Table 21-2 provides a mnemonic to help remember to "SNOOP for the red flags."

5. Which imaging modality—CT or MRI—is the preferred neuroimaging for the evaluation of headaches?
When available, MRI is the preferred study for the evaluation for headaches. CT is preferable in acute situations such as head trauma, acute headache to rule out subarachnoid hemorrhage, as well as in patients with contraindications to MRI.

Table 21-1 Key Questions to Ask for the Headache History

- Do you have different types of headaches or just one?
- Where does the headache hurt?
- When did you first start having these headaches?
- What were you doing when the headache started?
- How long before the headache reaches maximal intensity?
- How long does the headache last?
- Does the headache recur? If so, how often?
- What is the pain like? Is it a pressure, throbbing, pounding, aching, or stabbing?
- On a scale of 1 to 10, with 10 the worst and 1 the least, how would you rate the headache?
- Do you have trouble with your vision before or during the headache?
- Do you have other symptoms (e.g., nausea, vomiting, light sensitivity, noise sensitivity, cranial autonomic symptoms) with the headache?
- During a headache, would you prefer to be in bright sunlight or in a dark room?
- During a headache, would you prefer to be in a room with loud music or in a quiet room?
- Are signs present (e.g., fever, ptosis, miosis)?
- Do you have triggers of your headaches (e.g., menses, stress, foods, beverages, lack of sleep, oversleeping, strong odors, trigger zones)?
- What makes the headache worse (e.g., coughing, Valsalva, physical activity)?
- What makes the headache better (e.g., sleep, lying down in a quiet room)?
- Do your headaches have any impact on your life (missed work, school, family or social activities)?
- Do you take over-the-counter medications, vitamins, or herbs for your headaches? If so, how much and how often?
- Do you drink caffeinated beverages? If so, what types and how many?
- What prescription drugs have you tried, what doses, for what duration, and with what effect? Any side effects?
- What doctors have you seen in the past for your headaches?
- What other treatments have you tried and with what success (e.g., acupuncture, chiropractic, biofeedback, stress management, massage)?
- Have you been under much stress lately?
- Have you been depressed?
- Do you have any parents or siblings with a history of migraines or bad headaches?

From Evans RW: Diagnosis of headaches. In: Evans RW, Mathew NT, editors: Handbook of headache. 2nd ed. Philadelphia: Lippincott Williams & Wilkins, 2005, p. 1.

Table 21-2 SNOOP: Red Flags to Consider Neuroimaging for Headaches

- Systemic symptoms (fever, weight loss) or
  Secondary headache risk factors (HIV, systemic cancer, pregnancy and postpartum)
- Neurologic symptoms or abnormal signs (confusion, impaired alertness, or consciousness)
- Onset: sudden, abrupt, or split-second-thunderclap
- Older: new onset and progressive headache, especially in age >50 years (e.g., giant cell arteritis)
- Previous headache history or headache progression: first headache or different (change in attack frequency, severity, or clinical features)

Data from Dodick DW. Diagnosing headache: clinical clues and clinical rules. Advanced Studies in Medicine 3:87-92, 2003. (Galen Publishing)

The following causes of headache can be missed on a routine CT scan of the head: vascular disease (saccular aneurysms, arteriovenous malformations—especially posterior fossa), subarachnoid hemorrhage, carotid or vertebral artery dissections, infarcts, cerebral venous thrombosis, vasculitis (white matter abnormalities), cerebral vasospasm, and subdural and epidural hematomas; neoplastic disease (neoplasms especially in the posterior fossa, meningeal metastases, and pituitary tumor and hemorrhage), cervicomedullary lesions (Chiari malformations and foramen magnum meningioma); infections (paranasal sinusitis, meningoencephalitis, cerebritis, and brain abscess); and low cerebrospinal fluid (CSF) pressure syndrome.

CT of the head also exposes the patient to ionizing radiation (2 mSv without contrast) where there may be a delayed increased risk for various cancers with a greater potential for younger people (see www.xrayrisk.com).

PRIMARY HEADACHES

6. How do you distinguish between episodic migraine, tension type, and cluster headaches (CHs)?

Table 21-3 compares and contrasts these headaches.

Table 21-3 Features of Some Primary Headaches

FEATURE	EPISODIC MIGRAINE	EPISODIC TENSION TYPE	EPISODIC CLUSTER
Epidemiology	• 18% of women • 6% of men • 4% of children before puberty	• 90% of adults • 35% of children aged 3-11 years	• 0.4% for men • 0.08% for women
Female/male	• 3/1 after puberty • 1/1 before puberty	5/4	1/5
Family history	80% of first-degree relatives	Frequent	Rare
Typical age at onset	• 92% before age 40 • 2% after age 50	20-40	20-40
Visual aura	In 30%	No	Occasional
Location	• Unilateral, 60% • Bilateral, 40%	Bilateral > unilateral	Unilateral maximal orbital, supraorbital, and/or temporal
Quality	Pulsatile or throbbing in 85%	Pressure, aching, tight, squeezing	Boring, burning, or stabbing
Severity	Mild to severe	Mild to moderate	Severe
Onset to peak pain	Minutes to hours	Hours	Minutes
Duration	• 4-72 hours • 2-72 hours in children	Hours to days	15-180 minutes
Frequency	Rare to frequent	Rare to frequent	1-8 per day during clusters
Periodicity	Menstrual migraine	No	Yes. Average bouts 4-8 weeks Average 1 or 2 bouts yearly
Associated features	• Nausea in 90% • Vomiting in 30% • Light and noise sensitivity in 80%	Occasional nausea	• Ipsilateral conjunctival injection and/or lacrimation in 95% • Nasal congestion and/or rhinorrhea in 77% • Ptosis and miosis in 30% • Eyelid edema in 21%
Triggers	Present in 85%	Stress, lack of sleep	Alcohol, nitrates
Behavior during headache	Still, quiet, tries to sleep	No change	Often paces
Awakens from sleep	Can occur	Rare	Frequently

Data from Evans RW: Diagnosis of headaches. In: Evans RW, Mathew NT, eds: Handbook of Headache. 2nd ed. Philadelphia: Lippincott, Williams & Wilkins, 2005, pp. 14-15.

7. Can primary headaches awaken people from sleep or be present upon awakening in the morning?

Yes, often with migraine, CHs, tension type, paroxysmal hemicranias, and hypnic headache (see Question 55). Exploding head syndrome is a rare disorder where the person is awoken from sleep by a sensation of a momentary loud noise in the head lasting a few seconds without headaches (several reports of associated migraines), and 10% of these patients describe an associated flash of light. This disorder may occur at any age but is more common in those over the age of 50 years.

8. What are chronic daily headaches of long duration?

Chronic daily headaches are the primary headache disorders in which patients experience headaches lasting 4 or more hours per day (without treatment), 15 or more days a month for 3 or more months. This disorder affects 3% to 5% of the worldwide population. These headaches include chronic migraine, chronic tension-type headache, new daily persistent headache, and hemicrania continua. In contrast, chronic daily headaches of short duration (headaches lasting less than 4 hours per day untreated) are rare and include chronic CH, chronic paroxysmal hemicrania, and short-lasting unilateral neuralgiform headache attacks.

MIGRAINE

9. How common is migraine?

In a given year, migraine has a prevalence of 12% (17.1% in women and 5.6% in men). Annually, some 35 million people suffer migraine in the United States. The cumulative incidence of this disorder by age 85 years is 18.5% in men and 44.3% in women, with onset before the age of 25 years in 50% of cases, before the age of 35 years in 75%, and over the age of 50 years in only 2%. The median age of onset is 25 years. In children, approximately 8% of boys and 11% of girls have migraine. However, only about 56% of migraineurs know that they have migraine. They or their doctors have made a misdiagnosis of "sinus" or allergy headache, stress headache, or eye strain. Ninety percent of patients presenting to primary care physicians with recurrent headache meet the criteria for migraine.

9A. Is migraine more common in neurologists and family medicine physicians than in the general population?

Yes. The lifetime prevalence is 47% among male neurologists and 63% among females. The lifetime prevalence is even higher among male and female headache specialists, respectively, 72% and 82%. Another study found an increased lifetime prevalence of migraine among male and female family physicians, respectively, 37% and 61%. The reason for the higher prevalence is not certain, but possible explanations include the following: migraine is more common in the general population than studies suggest (physicians are better at self-diagnosis or recall of migraines); migraine is associated with a choice to become a physician; and occupational stress leads to migraine in susceptible individuals.

9B. Which US Presidents or First Ladies had migraines?

Jefferson had episodic severe headaches that may have been a migraine variant, episodic daily migraine. Lincoln, Grant, and Wilson were migraineurs. John Adams, Truman, Eisenhower, and Kennedy may have been migraineurs. First Ladies Abigail Adams, Lincoln, Eisenhower, and Kennedy all suffered from migraines. Grant, who treated some migraines with chloroform, had a severe migraine that immediately went away when he received a letter from Lee offering terms of surrender. To treat migraines and stomach cramps, Wilson's physician prescribed golf 6 days a week. He played at least 1200 rounds as president, perhaps as many as 1600, with an average score of 115. Nixon is cited as stating, "He also told the physician [White House physician Dr. Tkach] that he had never had a headache. He seemed to think headaches were imaginary—excuses for weak men…."

10. What are the phases of migraine?

The *prodrome* or *premonitory phase* occurs in about 80% of migraineurs and may precede the attack by hours or up to 1 or 2 days. Symptoms include changes in mental state (such as depression, hyperactivity, irritability, or drowsiness), neurologic symptoms (such as photophobia, phonophobia, and yawning), and general symptoms (such as stiff neck, food cravings, diarrhea, or constipation).

- *Aura* in about 30%
- *Headache* in most but not everyone
- *Resolution phase* or *postdrome* symptoms include changes in mood, weakness, tiredness, anorexia, irritability, and poor concentration ("mashed potato brain")

11. What are the clinical features of migraine without aura?

The location is easy to remember. Any part of the head or face may be affected, including the parietal region, the upper or lower jaw or teeth, the malar eminence, and the upper anterior neck. Pain is unilateral in 60% of cases and bilateral in 40%. Approximately 15% of migraineurs report so-called side-locked headaches in which migraine always occurs on the same side. The pain is often more intense in the frontotemporal and ocular regions before it spreads to the parietal and occipital areas. Throbbing pain is present in 85% of episodes of migraine, although up to 50% of patients describe steady pain during some attacks. As many as 75% of migraineurs report unilateral or bilateral tightness, stiffness, or throbbing pain in the posterior neck along with head pain. The neck pain can occur during the migraine prodrome, the attack itself, or the postdrome.

Migraines last 4 to 72 hours if left untreated or if unsuccessfully treated. One that persists for more than 72 hours is termed *status migrainosus.* In children and adolescents (aged under 18 years), attacks may last 2 to 72 hours and the pain is more often bilateral (usually frontotemporal) than in adults.

Without treatment, 80% of patients experience moderate to severe pain, and 20% have mild pain. Usually increased by physical activity or movement, the pain is associated with nausea in about 80% of episodes, vomiting in about 30%, photophobia in about 90%, and phonophobia in about 80%.

Table 21-4 provides the International Headache Society criteria for the diagnosis of migraine.

Table 21-4 Diagnostic Criteria for Migraine Without Aura

A. At least five attacks fulfilling criteria B-D
B. Headache attacks lasting 4-72 hours (untreated or unsuccessfully treated)
C. Headache has at least two of the following four characteristics:
   1. Unilateral location
   2. Pulsating quality
   3. Moderate or severe pain intensity
   4. Aggravation by or causing avoidance of routine physical activity (e.g., walking or climbing stairs)
D. During headache at least one of the following:
   1. Nausea and/or vomiting
   2. Photophobia and phonophobia
E. Not better accounted for by another ICHD-3 diagnosis

From Headache Classification Committee of the International Headache Society (IHS): The International Classification of Headache Disorders, 3rd edition (beta version), Cephalalgia 33(9):629-808, 2013.

12. How often do migraines occur, is there associated impairment, and what are the genetics?

A quarter of all migraineurs suffer four or more severe attacks a month, 35% have one to four severe attacks per month, 38% experience one or fewer severe attacks per month, and 37% have five or more headache days per month. In one study, during migraine attacks, most migraineurs (53.7%) reported severe impairment or the need for bed rest, whereas only 7.2% reported no attack-related impairment. Over a 3-month period, 35.1% of the migraineurs had at least 1 day of restricted activity related to headache.

About 70% of migraineurs have an affected first-degree relative. Genetic heterogeneity is present.

13. What are the common migraine triggers?

Migraine triggers are present in 76% of migraineurs. One study reported the following triggers from affected patients: stress, 89%; female hormones, 65%; not eating, 57%; weather, 53%; physical exhaustion or travel, 53%; sleep disturbance, 50%; perfume or odor, 44%; bright lights, 38%; neck pain; 38%; alcohol, 38%; smoke, 36%; sleeping late, 32%; heat, 30%; food, 27%; and exercise, 22%.

14. Why are migraines misdiagnosed as "sinus" headaches?

Migraineurs and some physicians misdiagnose headaches as "sinus" because the pain occurs in the face or forehead, a change in weather is a common trigger, and the presence of cranial autonomic symptoms seems like sinus symptoms.

Cranial autonomic symptoms in migraine are caused by parasympathetic activation of the sphenopalatine ganglion, which innervates the tear ducts and sinuses. At least one symptom is present in 56% of migraineurs, usually bilaterally, but is not usually present during each attack. The most common cranial autonomic symptoms are forehead/facial sweating, conjunctival injection and/or lacrimation, and nasal congestion and/or rhinorrhea.

15. Why are migraines misdiagnosed as stress or tension-type headaches?

Migraines are confused with stress or tension-type headaches, because migraine pain is commonly experienced in the neck at some point during the attack (75%) and is often triggered by psychological stress (80%).

16. What is the epidemiology of migraine with aura?

In a given year in the United States, the prevalence of migraine with aura is 5.3% in women (30.8% of female migraineurs) and 1.9% in men (32% of male migraineurs). As many as 81% of those having migraine with aura also have attacks of migraine without aura.

The reported age of onset is between a mean of 11.9 years (range, 4 to 17) and a mean of 21 years (range, 5 to 77). In one study, 54.9% of patients suffered less than one attack per month, and 9.7% reported more than three attacks per month.

17. What are the clinical features of migraine aura?

The visual aura is the most common, occurring in 99% of attacks, sensory (typically unilateral numbness, tingling, or pins and needles in the hand, which may spread to the face or either alone, can have unilateral tongue paresthesias) in 30%, and dysphasia (if the dominant hemisphere or can have slurred speech) in 20%. When more than one aura type occurs during an attack, symptoms typically follow one another in succession, beginning with visual, then sensory, and then dysphasia.

Migraine aura meets International Headache Society criteria when the duration is 5 to 60 minutes. A duration of longer than 1 hour but less than a week defines probable migraine with aura. Visual aura lasts more than 1 hour in 6% to 10% of migraineurs with aura.

Table 21-5 provides the International Headache Society criteria.

Table 21-5 Criteria for Migraine With Aura

Description
Recurrent attacks, lasting minutes, of unilateral fully reversible visual, sensory, or other central nervous system symptoms that usually develop gradually and are usually followed by headache and associated migraine symptoms.

Diagnostic Criteria
A. At least two attacks fulfilling criteria B and C
B. One or more of the following fully reversible aura
   Symptoms:
   1. Visual
   2. Sensory
   3. Speech and/or language
   4. Motor
   5. Brain stem
   6. Retinal
C. At least two of the following four characteristics:
   1. At least one aura symptom spreads gradually over ≥5 minutes, and/or two or more symptoms occur in succession
   2. Each individual aura symptom lasts 5-60 minutes
   3. At least one aura symptom is unilateral
   4. The aura is accompanied, or followed within 60 minutes, by headache
D. Not better accounted for by another ICHD-3 diagnosis, and transient ischemic attack has been excluded

Headache Classification Committee of the International Headache Society (IHS). The International Classification of Headache Disorders. 3rd ed (beta version). Cephalalgia 33(9):629-808, 2013.

18. Does the aura only occur before the onset of the headache?
Although many consider the migraine aura to be a distinct phase of the migraine attack preceding the headache, one prospective study found the aura phase occurring during the headache in 73% of patients. The aura may follow the headache in 3% to 8% of cases.

19. Can aura occur without headache?
Yes. This is termed *typical aura without headache* (acephalgic migraine), which may be more common with older age. Although usually just a visual aura, other aura symptoms may also occur. With the first or very short or prolonged episodes or when symptoms are just negative such as hemianopsia, other causes may need to be excluded.

20. What are the symptoms of the visual aura?
Fortification (looks like a fortified town as viewed from above) spectra or teichopsia ("seeing fortifications"), which is a jagged figure with fortification lines arranged at right angles to one another beginning from a paracentral area, may be experienced, which start in or adjacent to the center of the visual field in 50% or in the peripheral in 50% and then spread, leaving visual loss behind. There are often scintillations, which may be white or gray or have colors similar to a kaleidoscope in a semicircle or C shape surrounding the scotoma or area of visual loss. Scintillating scotomata are typically in one hemifield, with visual field defects beginning around fixation and spreading outward. Some patients may describe other phenomena including zigzag lines, flashes of bright light, or heat waves.

21. What distinguishes a migraine aura from cerebral ischemia and seizures?
Visual or sensory auras from migraine typically spread slowly across the visual field or body part followed by a gradual return to normal function in the areas first affected after 20 to 60 minutes. The onset of cerebral ischemic events is usually sudden with an equal distribution in the relevant vascular territory, although the affected area can expand stepwise if blood flow drops in additional vessels. The return of function in areas first affected while symptoms begin in newly affected areas occurs in migraine aura but not in ischemia or seizures.

Migraine aura often begins with positive phenomena such as shimmering lights, zigzags in vision, or tingling. It is then frequently followed minutes later by negative symptoms such as scotoma, numbness, or a loss of sensation. This symptom progression can also occur during seizures but usually with a faster progression of symptoms. This cycle from positive to negative symptoms is not typical of cerebral ischemia.

22. What is vestibular migraine (migrainous vertigo)?
Vestibular migraine has a lifetime prevalence of 1% in the general population. The vertigo can occur with (in 50%) or without a headache and can have a variable duration ranging from seconds (approximately 10%) to minutes (30%) to hours (30%) to several days (30%). Patients may describe lightheadedness, spinning, or a sensation of the environment spinning. For some patients, it may take weeks to recover fully from an attack. The attacks may occur days, months, or even years apart in an irregular fashion.

23. What is migraine with brain stem aura (formerly called basilar-type migraine)?
Migraine with brain stem aura is a rare disorder that usually affects patients aged 7 to 20 years and rarely presents in individuals older than 50 years. One study reported the following aura symptoms: vertigo, 61%; dysarthria, 53%; tinnitus, 45%; diplopia, 45%; bilateral visual symptoms, 40%; bilateral paresthesias, 24%; decreased level of consciousness, 24%; and hypoacusis, 21%. Visual symptoms—usually blurred vision, shimmering colored lights accompanied by blank spots in the visual field, scintillating scotoma, and graying of vision—may start in one visual field and then spread to become bilateral. The median duration of aura was 60 minutes (range, 2 minutes to 72 hours), with two or more aura symptoms always occurring.

24. How are episodic, intermittent, and chronic migraine defined?
Episodic migraine is 14 or fewer headache days per month, while chronic migraine is defined as 15 or more headache days (tension type-like and/or migraine-like) per month for 3 months or more having the features of migraine headache on at least 8 days per month.

Chronic migraine, or transformed migraine, is a complication of intermittent migraine, with 2.5% progressing yearly from episodic to chronic migraine. In the United States, 3.2 million people have chronic migraine and 80% are women. It may occur with or without medication overuse. The pain is often mild to moderate and not always associated with photophobia, phonophobia, nausea, or vomiting and may resemble a mixture of migraine and tension-type headaches with intermittent severe migraine-type headaches. Depression is present in 40% and anxiety in 30%.

24A. Who described the first case of chronic migraine?
In 1672, Thomas Willis (1621-1675) provided the first description of chronic migraine when he reported the case of the philosopher Anne, Viscountess Conway, who was also treated by William Harvey and Robert Boyle without benefit. (Lady Conway's disabling migraines inspired her concept that pain and suffering were purgative with the ultimate aim of restoring creatures to moral and metaphysical perfection.)

Willis gave our field its name in 1664 by coining the Greek term *neurologie* and also coining the terms *lobe, hemisphere, pyramid, peduncle, corpus striatum,* and *reflexion* (later reflex). He demonstrated the functional significance and provided the best illustrations of the circle of Willis in 1664.

Willis also described the differentiation between diabetes insipidus and mellitus and described meningococcal meningitis, general paralysis, Jacksonian epilepsy, myasthenia gravis, transient ischemic attacks, carotid occlusion with headache (Willis headache), narcolepsy, and bipolar disorder. He introduced the doctrine of the gray cortex as the source of cerebral activities and the white matter as a mass of connections. Next time you are at Westminster Abbey, visit his burial site.

25. What are the risk factors for transformation from episodic to chronic migraine?
Risk factors for transformation include medication overuse (especially opiates and barbiturate combinations), high caffeine consumption, female gender, stressful life events, anxiety, depression, baseline high-attack frequency, individuals with lower educational and socioeconomic levels, white patients, lifetime injuries to the head or neck, obesity, snoring, arthritis, and presence of cutaneous allodynia.

26. What is a common abnormality on MRI scans of the brain in migraineurs?
White matter abnormalities are present on MRI scans more often in migraineurs (variably reported in 12% to 46%) than in controls (2% to 14%). White matter abnormalities are foci of hyperintensity on both proton density and T2-weighted images in the deep and periventricular white matter due to either interstitial edema or periventricular demyelination of uncertain etiology.

27. What is medication overuse headache (MOH) or medication rebound?
MOH or medication rebound is defined as headache occurring on 15 or more days per month and developing as a consequence of regular overuse of acute or symptomatic headache medication for more than 3 months. It is present in about 1% to 2% of the population who have preexisting migraine or tension-type headache. MOH can result from the following: combination over-the-counter medications, triptans, or opiates 10 or more days per month. Some evidence suggests nonsteroidal antiinflammatory drug (NSAID) use 15 or more days per month may cause MOH; however, other evidence suggests NSAIDs may be used for migraine prevention. Caffeine-withdrawal headache may develop within 24 hours after regular consumption of caffeine in excess of 200 mg/day for more than 2 weeks. Some migraineurs benefit from avoiding caffeine completely.

28. How is MOH treated?
Overused medications can be tapered off. For those taking high-frequency butalbital combinations, phenobarbital 30 mg twice a day (bid) can be substituted for 2 weeks followed by 15 mg bid for 2 weeks (abrupt withdrawal can result in seizures). For those taking high doses of opioids, clonidine 0.1 to 0.2 mg three times a day titrated up or down based on symptoms or clonidine patch 0.1 to 0.2 mg/24 hours for 1 to 2 weeks.

Naproxen 500 mg bid may be used alone or can be combined with tizanidine starting at 2 mg at bedtime and titrating up to 16 mg at bedtime (for 6 weeks in one study) as tolerated. Steroids are probably not effective.

29. How effective are triptans (serotonin 1b/1d agonists) for acute migraine treatment?
Oral sumatriptan, almotriptan, eletriptan, rizatriptan, and zolmitriptan relieve the pain in about 65% to 70% with better efficacy than frovatriptan and naratriptan (Table 21-6). Sumatriptan subcutaneous (SC) 6 mg provides headache relief in 70% by 2 hours and 80% by 4 hours. Sumatriptan 20 mg nasal spray (NS) and zolimitriptan 5 mg NS are second fastest. Sumatriptan SC, NS, and iontophoretic transdermal patch are preferred for those with prominent nausea/vomiting or who do not respond to oral triptans. All acute medications are more effective when taken when the pain is mild.

Table 21-6. Available Triptan Preparations

DRUG (BRAND NAME)	FORMULATION	STRENGTHS (mg)
Almotriptan (Axert)	Tablets	12.5
Eletriptan (Relpax)	Tablets	40
Frovatriptan (Frova)	Tablets	2.5
Naratriptan (Amerge)	Tablets	1, 2.5
Rizatriptan (Maxalt)	Tablets	5, 10
	Orally disintegrating preparation* (Maxalt MLT)	5, 10
Sumatriptan (Imitrex)	Subcutaneous injection	6
	Tablets	25, 50, 100
	Nasal spray	5, 20
Sumatriptan/naproxen (Treximet)	Tablet	85/500
Zolmitriptan (Zomig)	Tablets	2.5, 5
	Orally disintegrating preparation* (Zomig ZMT)	2.5, 5
	Nasal spray	5

*Dissolves on the tongue; can be taken without water (efficacy similar to that of tablet form).
Modified with permission from Evans RW: Headaches. In: ACP Medicine, BC Decker, 2009.

30. What are contraindications to triptans? What about the risk of serotonin syndrome (SS)?
According to the package insert (PI), contraindications to use include those with ischemic heart disease, Prinzmetal's angina, Wolff–Parkinson–White syndrome or arrhythmias associated with other cardiac accessory conduction pathway disorders, cerebrovascular syndromes (including strokes and transient ischemic attacks), peripheral vascular disease (including ischemic bowel disease), uncontrolled hypertension, hemiplegic or basilar migraine, and use within 24 hours of ergotamine derivatives.

The PI also warns that SS may occur with 5-HT_1 agonists, particularly when used concomitantly with other serotonergic drugs. The American Headache Society's position paper concludes, "The currently available evidence does not support limiting the use of triptans with selective serotonin reuptake inhibitors or selective serotonin/norepinephrine reuptake inhibitors, or the use of triptan monotherapy, due to concerns for serotonin syndrome."

31. What is recurrence?
Recurrence refers to an initial reduction in pain intensity or resolution of pain of the acute migraine in response to analgesic treatment with subsequent pain recurrence within 24 hours. Its occurs depending on the initial analgesia used with a low of 14% of the time with a combination of sumatriptan and naproxen, 20% of the time with frovatriptan, and a high of 40% with sumatriptan SC.

32. What are emergency department (ED) options for treatment of severe migraine?
Five million visits to US EDs annually are due to patients with migraine. Intravenous hydration is important for those who have been vomiting.

The Canadian Headache Society systemic review strongly recommends use of the following: intravenous (IV) prochlorperazine 10 mg (which may be given with diphenhydramine 25 mg IV to prevent extrapyramidal side effects; diphenhydramine can also be given with metoclopramide); metoclopramide 10 mg IV; sumatriptan 4 to 6 mg SC (not used first line if another triptan has been taken in the past 24 hours); and ketorolac intramuscularly (IM) and IV 60 mg. Dihydroergotamine 0.5 mg IV with an antiemetic is a reasonable first-line option in the appropriate patient who has not had a triptan within 24 hours. Meperidine 75 to 100 mg IM is weakly recommended. The Society strongly recommends against the use of dexamethasone for the acute treatment of migraine pain.

33. How is menstrual migraine (MM) treated?
About 50% of female migraineurs report migraines with their menses, and 14% have MM only. Many women respond to the usual acute medications. For nonresponders, perimenstrual prevention with triptans may be effective beginning 2 to 3 days prior to the expected onset of the menses and continuing for a total of 5 days (frovatriptan 2.5 mg bid or zolmitriptan 2.5 mg three times a day [tid] or bid). Transcutaneous estradiol gel 1.5 mg or a 0.1 mg/24 h patch applied 2 days prior to the onset of menses and continued for 7 days may also be effective. For those with refractory MM or with irregular menses, daily migraine prevention can be tried. For those already using estrogen–progestin oral contraceptives, continuous contraception for 3 months or more can be effective.

34. What are indications for starting preventive medications in migraine?
The following factors may indicate the need for preventive medication treatment: recurring migraines that in the patient's opinion significantly interfere with daily routine, despite acute treatment; contraindication to or failure or overuse of acute therapies; adverse events with acute therapies; and patient preference. In addition to medication, triggers are avoided as much as possible, and adequate and regular sleep, avoiding missed meals, and regular exercise may be beneficial.

35. How are preventive medications used and which are effective for episodic migraine?
A preventive medication is slowly titrated to the target dose and taken for a minimum of 8 weeks to see if effective. Contraception should be discussed with women of childbearing potential and the potential risk of medication with pregnancy. A paper or electronic headache diary should be kept to monitor progress.

Table 21-7 provides the American Headache Society/American Academy of Neurology Migraine Prevention Guidelines. Choose a medication based upon efficacy, the patient's preferences, the medication side effects, and the presence or absence of coexisting or comorbid conditions. One medication may be used for migraine and another disorder, a "two for" (such as depression, epilepsy, or hypertension). The most effective medications reduce the frequency of headaches by about 50% in about 50% of migraineurs.

36. How well are preventive medications tolerated?
Perhaps 20% of patients discontinue each of the preventive medications due to side effects. The physician should discuss the side effect profile with the patient before starting. For example, divalproex can cause nausea, somnolence, tremor, dizziness, weight gain, and hair loss. Caution should be used in prescribing divalproex or any valproic acid derivative to women of childbearing potential because of the risk for teratogenicity including major malformations and adverse cognitive and developmental outcomes. Topiramate can cause paresthesias, changes in taste (soft drinks may taste flat), depression, kidney stones in about 1%, reversible cognitive impairment in about 10%, weight loss, and rarely glaucoma.

37. Are alternative or nonmedication treatments effective for episodic migraine prevention?
Relaxation training, thermal biofeedback combined with relaxation training, electromyographic biofeedback, and cognitive behavioral therapy have grade A evidence for prevention of migraine. Acupuncture may be helpful. The evidence is inconclusive for spinal manipulation.

Regular aerobic exercise may be helpful. Weight loss may help to reduce the frequency of migraines in overweight patients. Treatment of insomnia and obstructive sleep apnea may also be helpful.

38. What medications are effective for chronic migraine prevention?
The evidence for efficacy of preventive medication is different for chronic migraine than for episodic migraine (Table 21-8).

39. What is dihydroergotamine (DHE) IV transitional therapy and what is its efficacy?
For those with refractory chronic migraine, 67% have headache attack freedom during treatment and 75% have headache freedom within 1 month of completion, with duration of effect of an average of 28 days. DHE has the same contraindications as triptans.

Table 21-7 AHS/AAN Migraine Prevention Guidelines 2012

Drugs Recommended for Use

DRUG	EXAMPLES OF STUDIED DOSES
Level A: Established as Effective	
Should be offered to patients requiring migraine prophylaxis	
Divalproex/sodium valproate	400-1000 mg/day
Metoprolol	47.5-200 mg/day
Petasites (butterbur)*	50-75 mg bid
Propranolol	120-240 mg/day
Timolol	10-15 mg bid
Topiramate	25-200 mg/day
Level B: Probably Effective	
Should be considered for patients requiring migraine prophylaxis	
Amitriptyline	25-150 mg/day
Fenoprofen	200-600 mg tid
Feverfew	50-300 mg bid; 2.08-18.75 mg tid for MIG-99 preparation
Histamine	1-10 ng subcutaneously twice a week
Ibuprofen	200 mg bid
Ketoprofen	50 mg tid
Magnesium	600 mg trigmagnesium dicitrate qd
Naproxen/naproxen sodium	500-1100 mg/day for naproxen 550 mg bid for naproxen sodium
Riboflavin	400 mg/day
Venlafaxine	150 mg extended release/day
Atenolol	100 mg/day
Level C: Possibly Effective	
May be considered for patients requiring migraine prophylaxis	
Candesartan	16 mg/day
Carbamazepine	600 mg/day
Clonidine	0.75-0.15 mg/day; patch formulations also studied
Guanfacine	0.5-1 mg/day
Lisinopril	10-20 mg/day
Nebivolol	5 mg/day
Pindolol	10 mg/day
Flurbiprofen	200 mg/day
Mefenamic acid	500 mg tid
Coenzyme Q10	100 mg tid
Cyproheptadine	4 mg/day

Data from Silberstein SD, Holland S, Freitag F, et al.; Quality Standards Subcommittee of the American Academy of Neurology and the American Headache Society. Evidence-based guideline update: pharmacologic treatment for episodic migraine prevention in adults: report of the Quality Standards Subcommittee of the American Academy of Neurology and the American Headache Society. Neurology 78(17):1337, 2012.

*Advise patients of rare risk of hepatotoxicity and monitor liver function tests if they wish to assume risk of use. Don't use in children and pregnancy. (Tepper SJ. Nutraceutical and Other Modalities for the Treatment of Headache. Continuum. 2015;21(4):1018-31).

Table 21-8 Preventive Medications for Chronic Migraine With Target Doses or Dose Ranges

Randomized Controlled Trials
OnabotulinumtoxinA 155 units (FDA approved)
Topiramate 100-200 mg daily
Divalproex sodium 500 mg bid
Gabapentin 800 mg tid
Tizanidine 8 mg tid
Amitriptyline 100 mg daily
Fluoxetine 40 mg daily
Candesartan 16 mg daily
Propranolol 160 mg long acting daily

Open Label
Pregabalin 150 mg bid
Zonisamide 100-400 mg daily
Atenolol 50 mg daily
Olanzapine 2.5-35 mg daily
Methylergonovine maleate 0.2-0.4 mg tid
Memantine 10-20 mg daily in divided doses
Combined?
Anecdotal
Venlafaxine 150 mg extended release daily

From Evans RW: An update on the management of chronic migraine. Pract Neurol November/December, 27-32, 2013. *Available at http://practicalneurology.com/pdfs/PN1113_SF_ChronicMigraine.pdf.*

Pretreatment is given with 4 mg of ondansetron (obtain baseline electrocardiogram risk of QT prolongation, pregnancy test as appropriate—some clinicians prefer metoclopramide 10 mg IV instead) before each dose of DHE (no triptan for 24 hours before). Day 1: DHE 0.5 mg in 100 mL of normal saline IV over 1 hour. If well tolerated (if not tolerated, dose is not titrated up or can be decreased to a lower dose), second dose 8 hours later of 0.75 mg in 250 mL of normal saline IV over 1 hour. Days 2 to 5: third and subsequent doses 1 mg in 250 mL of normal saline over 1 hour IV every 8 hours with the goal of a cumulative total dose of 11.25 mg (±1 mg) over 5 days.

For moderate or severe nausea, options are an additional dose of ondansetron 4 mg IV every 8 hours as necessary or promethazine 12.5 to 25 mg IV every 12 hours. DHE can also be given over 2 to 3 hours or the dose decreased or not escalated. Ketorolac 30 mg IV every 12 hours prn headache can be used for 3 days.

Some clinicians use IV valproate when DHE is contraindicated or in addition to DHE (loading dose of 15 mg/kg infused over 30 minutes followed by 5 mg/kg infused over 15 minutes every 8 hours).

TENSION-TYPE HEADACHES

40. How common are tension-type headaches and what are the clinical features?

The 1-year prevalence of the episodic type is 38% and chronic (15 or more days per month for 3 or more months) is 2%. Most have headaches less than 1 day per month.

The typical headache is a bilateral mild to moderate intensity, nonthrobbing headache described as dull, pressure, a tight cap, band, or a heavy pressure without associated symptoms. The headache is unilateral in 10% and occasionally pulsating. Stress is a common trigger.

41. How are tension-type headaches treated?

For acute treatment, most patients respond to over-the-counter medications such as NSAIDs and simple analgesics that may be combined with caffeine. Opioids and butalbital combinations should be avoided.

Preventive treatment is indicated for those with frequent or chronic tension-type headaches. Amitriptyline (nortriptyline and protriptyline are alternatives) is started at 10 to 25 mg at bedtime and titrated to a target dose of 100 mg as tolerated. Studies also suggest benefit from the use of mirtazapine, venlafaxine, topiramate, and gabapentin. Biofeedback and relaxation techniques may also be beneficial.

Trigeminal Autonomic Cephalalgias

42. What are the trigeminal autonomic cephalalgias (TACs)?
TACs are a group of primary headache disorders characterized by unilateral trigeminal distribution pain that occurs in association with prominent ipsilateral cranial autonomic features. TACs include CH, paroxysmal hemicrania, short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing (SUNCT), short-lasting unilateral neuralgiform headache attacks with cranial autonomic symptoms (SUNA), and hemicrania continua. Table 21-9 provides a comparison of the clinical features of the shorter duration TACs. These are typically diagnoses of exclusion with neuroimaging (preferably MRI scans including the pituitary) to exclude secondary causes.

Table 21-9. Clinical Features of the Trigeminal Autonomic Cephalalgias

	CLUSTER HEADACHE	PAROXYSMAL HEMICRANIA	SUNCT SYNDROME	HEMICRANIA CONTINUA
Sex F:M	1:3.5–7	2.13–2.36:1	1:2.1	2.4:1
Pain				
Type	Stabbing, boring	Throbbing, boring, stabbing	Burning, stabbing, sharp	Background dull ache, throbbing/stabbing exacerbations
Severity	Excruciating	Excruciating	Severe	Moderate background pain; severe exacerbations
Site	Orbit, temple	Orbit, temple	Periorbital	Orbit, temple
Attack frequency	1 every other day–8 daily	1–40/day	1/day–30/hr	Continuous
Duration of attack	15–180 min	2–45 min	5–250 seconds	Continuous background pain; exacerbations quite variable and lasting minutes to days
Autonomic features	Yes	Yes	Yes (prominent conjunctival injection and lacrimation)	Yes—mainly with exacerbations; less prominent than with other TACs
Migrainous features*	Yes	Yes	Yes†	Yes—during exacerbations
Alcohol trigger	Yes	Occasional	No	Rare
Indomethacin effect	–	++	–	++
Abortive treatment	Sumatriptan injection or nasal spray Oxygen	Nil	Nil	Nil
Prophylactic treatment	Verapamil Methysergide Lithium Prednisolone	Indomethacin	Lamotrigine Topiramate Gabapentin	Indomethacin

TACs, Trigeminal autonomic cephalalgias.
*Nausea, photophobia, or phonophobia.
†Photophobia homolateral to pain.
From Goadsby PJ. Migraine and the trigeminal autonomic cephalagias. In: McMahon SB, Koltzenburg M, Tracey I, et al., editors. Wall & Melzack's Textbook of Pain, 6th ed. Philadelphia: Elsevier; 2013. p. 815–831.

Hemicrania Continua

43. What is hemicrania continua (HC)?
HC is a rare disorder that may have a prevalence of up to 1% of the population. HC is more common in females than males, 1.6:1. The onset is often during the third decade of life with a range from the first to seventh decades.

The pain is strictly unilateral most commonly in the orbital, frontal, and temporal areas but can be occipital or other areas of the head or neck. The pain can be mild to severe throbbing or sharp. The pain is typically constant, but 20% have pain-free periods for 1 day to several months. Exacerbations occur in 75% of patients and typically last 20 minutes to several days. The pain can be associated with nausea, vomiting, light and noise sensitivity, and rarely a visual aura. Cranial autonomic symptoms, most commonly tearing and conjunctival injection, occur in 75% of patients. HC is a mimic of chronic migraine.

44. What is the treatment for HC?
HC is defined by the fact that is resolves completely with indomethacin. One regimen is the following: 25 mg three times a day for 3 days, subsequently increasing, if ineffective, to 50 mg three times a day for a further 3 days and then, if ineffective, to 75 mg three times per day for 3 days. The lowest effective dose is continued. Because of the risk of gastroduodenal mucosal injury, indomethacin is typically taken with a proton pump inhibitor.

For those who cannot tolerate indomethacin, other treatments, although much less effective, include topiramate, melatonin 6 to 12 mg at bedtime, verapamil, and gabapentin.

Cluster Headaches

45. What is the epidemiology of CH?
The lifetime prevalence is about 0.1% and the 1-year prevalence is 53 per 100,000, with a male to female ratio of 4:1. Onset is typically from ages 20 to 40 years although the range is from 4 to 96 years, with onset occurring after the age of 50 years in 10% of cases.

Five to 20% have a family history. The risk of CH for first-degree relatives is increased by 14- to 39-fold. Up to 85% of patients are chronic cigarette smokers, but quitting smoking has no effect on the disease. During cluster periods, trigger factors include alcohol ingestion and nitric oxide donors or promoters such as nitroglycerin or sildenafil.

46. What are the clinical features of CH (Table 21-10)?
The strictly unilateral pain is behind the eye in about 90%, over the temple in 70%, and over the maxilla in 50% although the pain may be in the occipital neck region. The pain is usually severe in intensity and is sharp, stabbing, piercing, burning, or pulsating in quality. Most have one to three attacks per day. About 15% report that the pain shifts sides between bouts of attacks and, less often,

Table 21-10. Diagnostic Criteria for Cluster Headache

A. At least five attacks fulfilling criteria B-D
B. Severe or very severe unilateral orbital, supraorbital, and/or temporal pain lasting 15-180 minutes (when untreated)*
C. Either or both of the following:
   1. At least one of the following symptoms or signs, ipsilateral to the headache:
      a. Conjunctival injection and/or lacrimation
      b. Nasal congestion and/or rhinorrhea
      c. Eyelid edema
      d. Forehead and facial sweating
      e. Forehead and facial flushing
      f. Sensation of fullness in the ear
      g. Miosis and/or ptosis
   2. A sense of restlessness or agitation
D. Attacks have a frequency between one every other day and eight per day for more than half of the time when the disorder is active
E. Not better accounted for by another ICHD-3 diagnosis

*During part (but less than half) of the time course of cluster headache, attacks may be less severe and/or of shorter or longer duration.

during a bout, but never during a single attack. Untreated, each headache lasts 15 to 180 minutes, during which patients usually are either restless or agitated and prefer to pace, rock back and forth, or bang their heads. Nocturnal attacks occur in 70%.

Migrainous symptoms of light and noise sensitivity are reported by 70%, vomiting or nausea in more than 20%, and perhaps 14% report an aura (including visual and paresthesia). About 97% have ipsilateral cranial autonomic symptoms such as conjunctival injection, lacrimation, nasal congestion and/or rhinorrhea, eyelid edema, ptosis, and miosis.

47. How often do attacks of CHs occur and what is the difference between episodic and chronic CHs?

An "attack" is a single attack of pain, and a bout is a series or "cluster" of attacks. In the absence of preventive medications, episodic CH is characterized by bouts lasting 7 days to 1 year separated by remission periods lasting 1 month or longer. Chronic CH is the absence of remission for 1 year or remissions of less than 1 month. Ten percent of CH is the chronic type. Chronic CH may either be chronic from onset or may evolve from the episodic type.

Most people have one bout per year, with a mean bout duration of 8.6 weeks. Some patients can go years without a bout, and others have frequent bouts each year.

48. What is the acute and transitional treatment for CH?

Triptans, especially subcutaneous sumatriptan 4 to 6 mg, are the mainstay of treatment. Subcutaneous sumatriptan can result in pain freedom within 20 minutes in 75% of CH suffers. Intranasal zolmitriptan 5 mg and sumatriptan 20 mg may be effective but less so than subcutaneous sumatriptan. Anecdotally, some patients report benefit from oral triptans. Dihydroergotamine 1 mg IM or 2 mg intranasally may also be effective. Inhalation of 100% oxygen administered through a nonrebreather face mask at a rate of 8 to 15 L/min for 15 to 20 minutes with the patient sitting upright is effective in about 80% of cases.

Some patients with episodic and chronic CH benefit from transitional or bridging therapy resulting in a temporary remission while waiting for either a preventive medication to work or for the bout to end. One regimen anecdotally suggested is prednisone 60 mg daily for 5 days and then tapered by 10 mg daily. Ipsilateral greater occipital nerve block with steroid and local anesthetic has also been reported as effective.

49. What preventive treatment is effective for CH?

Verapamil is the drug of choice for both episodic and chronic types. It is started at 120 to 240 mg a day and slowly increased (80-mg increase every 3 to 7 days as tolerated) to 480 mg if necessary. High doses may be required (maximum dose 960 mg/day) depending upon tolerability and response. The drug can be given in both a regular formulation three times daily and an extended-release formulation once a day although, anecdotally, the three-times-daily dosing may be more effective. With daily doses of 240 mg or higher, baseline and serial electrocardiograms, repeating the electrocardiograms 1 to 2 weeks after a dose change, usually in 80-mg increments, are indicated to monitor for the development of heart block, which becomes more frequent at higher doses.

Topiramate may be effective (starting at 25 mg/day and titrating up to 100 mg/day). Valproic acid is questionably effective. Melatonin is questionably helpful as a CH preventive. Lithium may be effective for chronic and episodic CHs typically starting at 300 mg bid or tid and increasing every 4 to 5 days based upon levels, with a typical maintenance dose of 900 to 1200 mg daily in three to four divided doses. The lithium plasma level should be monitored and kept between 0.6 and 1.2 mmol/L. Lithium has a narrow therapeutic window and numerous significant side effects.

Other Primary Headaches

50. What is primary cough headache?

Primary cough headache, which has a lifetime prevalence of 1%, is a sudden-onset bilateral or unilateral headache lasting seconds to 2 hours without associated symptoms provoked by coughing, sudden postural movements, weightlifting, laughing, and defecating and usually occurring in people over the age of 40 years. Secondary pathology should be excluded including Chiari type 1 malformation, posterior fossa lesions, unruptured cerebral aneurysms, spontaneous intracranial hypotension, and subdural hematoma by obtaining an MRI of the brain with and without contrast, and MRA (magnetic resonance angiogram) of the brain.

The cough should be treated. Indomethacin 50 to 200 mg daily in divided doses can be very effective (combined with a proton pump inhibitor for prolonged use). Acetazolamide, topiramate, propranolol, and naproxen may also be effective.

51. What is primary exercise headache?

Primary exercise headache may occur in 10% of the population and is a typically bilateral throbbing headache lasting from minutes up to 48 hours brought on by or occurring only during or after sustained physical exercise not usually associated with nausea and vomiting although migraineurs may have exercise as a trigger. The average age of onset is 24 (±11) years. Secondary pathology such as space occupying lesions and vascular pathology should be excluded with an MRI of the brain and MRA of the brain and neck.

Indomethacin 25 to 150 mg in divided doses can be taken daily for dosing 30 to 60 minutes before exercise for prevention. Propranolol and naproxen may also be effective.

52. What is primary headache associated with sexual activity?

With a lifetime prevalence of 1%, this is a bilateral (33% unilateral) occipital or diffuse headache lasting from 1 minute to 24 hours with severe intensity and/or up to 72 hours with mild intensity. The preorgasmic headache is a dull, usually bioccipital pressure or aching occurring during sexual activity and increasing in intensity with increasing sexual excitement. Orgasmic headache has a sudden explosive onset followed by a severe throbbing generalized headache.

Secondary causes of headache such as subarachnoid hemorrhage, arterial dissection, reversible cerebral vasoconstriction syndrome, hemorrhage into a cerebral tumor, and pheochromocytoma should be excluded with testing such as an MRI of the brain and MRA of the brain and neck or other appropriate studies. Approximately 5% of aneurysmal subarachnoid hemorrhages occur during sex.

Triptans may be effective for acute treatment. For prevention, triptans can be taken 30 minutes to 4 hours before sexual activity (depending upon the half-life of the triptan, e.g., sumitriptan 20 mg NS 30 minutes before, sumatriptan 100 po 2 hours before, and frovatriptan 2.5 mg 4 hours before). Indomethacin (25 to 225 mg per day), propranolol (40 to 240 mg per day), and topiramate (titrated to 100 mg daily) may be effective for prevention.

53. What is primary thunderclap headache?

A thunderclap headache is a severe headache of sudden onset reaching maximum intensity in less than 1 minute and lasting 5 minutes. A secondary headache must be excluded with appropriate testing, especially subarachnoid hemorrhage, which is the cause of up to 25% of thunderclap and sentinel headaches. Headache after subarachnoid hemorrhage typically lasts at least an hour or two.

These disorders present with thunderclap headaches the following percentages of the time: reversible cerebral vasoconstriction syndrome, 85%; cervical artery dissection, 20%; spontaneous intracranial hypotension, 15%; and cerebral venous thrombosis, 2% to 10%. There are numerous other causes including pituitary apoplexy, retroclival hematoma, ischemic stroke, acute hypertensive crisis, colloid cyst of the third ventricle, meningitis, complicated sinusitis, and subdural hematoma.

54. What is primary stabbing ("ice pick") headache?

An idiopathic disorder with transient and localized stabs of pain lasting 3 seconds or less 80% of the time (rarely 10 to 120 seconds) anywhere on the head, unilateral > bilateral of mild to severe intensity occurring in children and adults. One study found 38% with single stabs, 30% with a series of stabs, and 32% with both. This disorder is comorbid with migraine as well as tension-type headache, hemicrania continua, and primary cough headache.

Secondary causes of short stabbing headaches include herpetic meningoencephalitis, intracranial meningioma, pituitary tumors, acute thalamic hemorrhage, temporal arteritis (age >50 years), multiple sclerosis, systemic lupus erythematosus, Sjogren's, Behçet's, vasculitis, Lyme, and antiphospholipid antibody syndrome.

Possible treatments include indomethacin 75 to 150 mg daily, celecoxib 100 mg bid, melatonin 3 to 12 mg daily, gabapentin, and botulinum toxin A injections as well as amitriptyline in children.

55. What is hypnic headache?

Hypnic headache is a rare disorder that occurs in patients over the age of 50 years in 92% (rarely in children). Females are affected 65% of the time. The headache occurs only during sleep and awakens the sufferer at a consistent time (often 2 to 4 am). Nausea is infrequent and autonomic symptoms are uncommon. The headache can be unilateral or bilateral, throbbing or nonthrobbing, and mild to severe in intensity. The headache's duration can range from 15 minutes to 10 hours, with most lasting less than 3 hours, and can occur frequently, as often as nightly, for many years.

The best treatments are caffeine (one cup of strong caffeinated coffee or a 40- to 60-mg caffeine tablet before bedtime—insomnia is usually not reported in these patients), lithium carbonate (150 to 600 mg at bedtime), and indomethacin 25 to 50 mg tid and then tapering off after several weeks. A number of other medications have been reported as effective in case reports.

56. What is new daily persistent headache (NDPH)?

NDPH is a rare, idiopathic, persistent headache with pain becoming continuous and unremitting within 24 hours of onset, present for more than 3 months. Most patients have a constant headache ranging from mild to severe and bilateral in 89%, and present in any head region. Migraine features are present in over 50%. The age of onset ranges from 6 to greater than 70 years. Preceding stressful life events are reported in 10%, a flu-like, upper respiratory infection in 14% to 30%, and extracranial surgery in 7% to 12%.

NDPH is a diagnosis of exclusion including neoplasms, chronic subdural hematoma, post-traumatic, spontaneous intracranial hypotension, idiopathic intracranial hypertension, cervical artery dissection, reversible cerebral vasoconstriction syndrome, cerebral venous thrombosis, arteriovenous malformation, dural arteriovenous fistula, sphenoid sinusitis, chronic meningitis, postmeningitis, Chiari malformation, temporal arteritis, cervicogenic, and greater occipital neuralgia. The headache is treated like the primary headache (migraine or tension type) it most resembles.

SECONDARY HEADACHES

57. What are the features of secondary headaches?

Table 21-11 compares and contrasts the features of selected secondary headaches.

58. What are the features of posttraumatic headaches (PTH)?

Headaches occur in 30% to 90% of those symptomatic after mild traumatic brain injury. The prevalence and lifetime duration are greater in those who have mild head injury compared with those who have more severe injury. According to ICHD-3, the onset should be within 7 days of trauma or injury or within 7 days of regaining consciousness and/or the ability to sense and report pain when these abilities have been lost.

In most civilian studies, migraine-type headaches occur in about 25% while in US military series after blast trauma, migraine type is reported by about 75%. In one study of PTH in athletes, migraine type was reported by 18%. The other headaches are predominantly tension type. PTH can also be due to occipital neuralgia, supra- and infraorbital neuralgia, scalp lacerations, and temporomandibular disorder. Rare causes include TACs, CSF leaks through a cribiform plate fracture, cervical arterial dissections, cerebral venous thrombosis, and carotid-cavernous fistula. Of course, subdural and epidural hematomas should be excluded.

59. What are the prognosis and treatment of PTH?

Persistent headaches are reported at 3 months in 47% to 78%, 1 year in 8.4% to 35%, and 4 years in 24%.

There are few randomized, placebo-controlled trials of medications. The headaches are treated like the primary headache it most resembles.

60. What is footballer's migraine?

Minor head trauma can sometimes trigger migraine attacks in migraineurs. Matthews reported migraine with aura sometimes repeatedly triggered by heading the ball in soccer in four young males (including a 12-year-old) and a 20-year-old boxer after being hit in the head.

The most famous example occurred in American football in the first quarter of Super Bowl XXXII viewed by 800 million when migraineur Terrell Davis of the Broncos was kicked in the helmet and developed a migraine with visual aura. He was taken out of the game and treated with his usual medication, DHE nasal spray. He returned headache free for the second half and had 20 carries for 90 yards, a Super Bowl record; three rushing touchdowns; and won the game's MVP award.

Early treatment of migraine can get your patients back to school or work or even enable them to be a Super Bowl MVP.

61. Do headaches occur with cerebral ischemia?

Headache is present with acute ischemic stroke or transient ischemic attack about 25% of the time and is more common with hemispheric rather than lacunar. The pain can be dull or throbbing and is more often unilateral to the side of the lesion, but it can be generalized. The mean duration of headache is 3.8 ± 2.1 days.

62. What is a sentinel headache?

A sentinel headache is a sudden, severe headache occurring preceding major aneurysmal subarachnoid hemorrhage by days or weeks in 10% to 43% of cases. The sentinel headache may be due to minor aneurysmal bleeding or expansion of the aneurysmal wall. Sentinel headache is not associated with neck stiffness, altered levels of consciousness, or focal neurologic signs.

63. What are the features of headaches occurring with cervical artery dissection?

The incidence of dissections is 2.6/100,000/year. Headache or neck pain is the only symptom of spontaneous cervical artery dissection in 8%. The headache has a thunderclap onset in about 20% of cases. Headache occurs in 60% to 95% of those with internal carotid artery dissection (ICAD) preceding other neurologic symptoms and/or signs by a mean time of 4 days. The pain of ICAD, which is ipsilateral in 91% of cases, is typically localized to the frontal or temporal area, jaw, ear, and/or orbit and is more often aching than throbbing. A partial Horner's syndrome occurs in about 25% of cases with ptosis and miosis.

Headache occurs in 70% of those with vertebral artery dissection (VAD) with head or neck pain preceding other neurologic symptoms and/or signs by a mean time of 14.5 hours. VAD is typically an ipsilateral occipitonuchal throbbing or pressure but can be bilateral.

64. What types of headaches occur with reversible cerebral artery vasoconstriction (RCVS)?

About 60% of patients develop the syndrome either postpartum or after exposure to vasoactive drugs (cannabis, ecstasy, selective serotonin reuptake inhibitors, triptans, cocaine, amphetamine, intravenous immunoglobulin). This type of headache occurs more commonly in women (3:1) and typically presents between the ages of 20 and 50 years (range 10 to 76 years). Multiple thunderclap can be associated with nausea and/or vomiting. Photophobia is a presenting feature in 94% of cases. Multiple thunderclap headaches may occur over a mean period of 1 week and may occur spontaneously or be triggered by cough, exertion, or Valsalva. One of the defining features of RCVS is transient cerebral vasoconstriction, which resolves within 1 to 3 months. Rare patients may develop NDPH.

Complications of RCVS include cervical artery dissection (12%), ischemic or hemorrhagic stroke (6% to 30%), cortical subarachnoid hemorrhage (22% to 34%), posterior reversible encephalopathy syndrome (9%), and seizures (3% to 9%). Nimodipine, nifedipine, and verapamil have been used. However, there are no placebo-controlled trials.

65. What are the symptoms of postdural puncture headaches (PDPH) and how can they be prevented?

PDPH are typically bilateral frontal, occipital, or generalized pressure-like or throbbing headaches, worse when upright, which can be associated with nausea, vomiting, dizziness, tinnitus, neck stiffness, and visual symptoms. They occur up to 40% of the time following diagnostic lumbar punctures, usually within 6 to 72 hours of the procedure. In 80% of patients the headache lasts less than 5 days but rarely can last for up to 1 year.

Risk factors include female gender, ages 18 to 30, smaller body mass index, prior chronic or recurrent headaches, prior PDPH, use of a Quincke needle, a larger diameter needle, perpendicular orientation of the bevel, and not reinserting the stylet. Atraumatic needles (such as the 22-gauge Sprotte or Whitache) greatly reduce the frequency of PDPH. Bed rest following lumbar puncture does not reduce the frequency of PDPH.

Bed rest is the initial treatment. Oral caffeine 300 mg every 6 to 8 hours might help temporarily. Caffeine sodium benzoate 500 mg in 1000 mL normal saline over 1 hour followed by 1000 mL of normal saline over 1 hour may relieve the headache in perhaps 50%. Persistent headaches can be treated with a lumbar epidural blood patch.

66. What are the features of headache due to spontaneous intracranial hypotension (SIH) or low CSF volume syndromes?

SIH almost always results from spontaneous CSF leaks, typically at the spinal level (most commonly thoracic) and rarely at the skull base. The annual incidence may be 5/100,000 cases, with a peak age of onset of 40 years and a female-to-male ratio of 1.5:1. It can occur in patients of all ages.

Orthostatic headache (a headache while upright, relieved while lying down) is the most common clinical manifestation. The headache may either appear or be relieved after a change in posture. The headache may be dull, throbbing, or pressure-like, mild to severe in intensity, and is usually but not always bilateral. The headache can be frontal, fronto-occipital, generalized, or occipital. It can gradually evolve into a nonorthostatic chronic daily headache or be a nonorthostatic chronic daily headache from onset. Other, less common types include exertional headaches, cough headaches, acute thunderclap onset, second-half-of-the-day headaches, paradoxical orthostatic headaches (present in recumbency, relieved when upright), intermittent headaches, and the acephalgic form (no headaches).

HEADACHE TYPE	EPIDEMIOLOGY	AGE OF ONSET	LOCATION	QUALITY AND SEVERITY	FREQUENCY	ASSOCIATED FEATURES	COMMENTS
Trigeminal neuralgia	4.3/100,000/year; 60% females	Usually >40 years; if <40 years, consider multiple sclerosis	Unilateral, 97%; second or third trigeminal division greater than first	Stabbing; electrical bursts; burning; lasts few seconds to <2 min	Few to many a day	Trigger zone present in 91% of cases	Usually due to vascular compression of CN V; scan needed to exclude occasional tumor
Brain tumor	Persons/year; 41,000 primary (1/3 malignant), 150,000 metastatic	Any age	Often bifrontal, unilateral or bilateral; any location	Can be pressure or throbbing, mild to severe	Occasional to daily; usually progressive	Papilledema in 40%; at time of diagnosis, headache present in 30-70%	Primaries in adults; lung, 64%; breast, 14%; unknown, 8%; melanoma, 10%; colorectal, 3%; hypernephroma, 2%
Idiopathic Intracranial Hypertension (pseudotumor cerebri)	1-2/100,000/year; 90% are female; 90% are obese	Mean of 30 years	Often bifrontotemporal but can occur in other locations and unilaterally	Pulsatile; moderate to severe	Daily	Papilledema in 95%; transient visual obscurations in 70%; intracranial noises in 60%; VI nerve palsy in 20%	MRI scan preferred to better exclude cortical venous thrombosis and posterior fossa lesions
Subarachnoid hemorrhage	30,000/year caused by saccular aneurysm	Mean of 50 years	Usually bilateral; any location	Usually severe but can be mild and gradually increasing in 19%	Paroxysmal	Often with nausea, vomiting, stiff neck, focal findings, syncope; stiff neck absent in 36%	CT scan abnormal on first day in 95%; third day, 74%; 1 week, 50%; lumbar puncture may be essential for diagnosis
Temporal arteriti	In age >50 years, annual incidence of 18/100,000; female-to-male ratio. 3:1	Rare before 50 years; mean age of 70 years	Variable, unilateral, or bilateral; often temporofrontal	Often throbbing; may be sharp, dull, burning, or lancinating; mild to severe	Intermittent to continuous	50% have PMR; jaw claudication in 38%; 50% have absent pulse or tender STA	ESR WNL in up to 36%; CRP usually elevated; STA biopsy false negative in up to 44%

Table 21-1 Features of Selected Secondary Headaches—cont'd

HEADACHE TYPE	EPIDEMIOLOGY	AGE OF ONSET	LOCATION	QUALITY AND SEVERITY	FREQUENCY	ASSOCIATED FEATURES	COMMENTS
Acute paranasal sinusitis	More common in children (in whom frontal and sphenoid sinusitis is rare) than in adults	Any age	Frontal (forehead), maxillary (cheek), ethmoid (between eyes), sphenoid (variable)	Dull, aching; can be severe	Acute lasts from 1 day to 3 weeks	Fever in about 50%; nasal congestion and purulent nasal drainage usually present (less often in sphenoid)	Well visualized on routine MRI but not on routine head CT scan; sinus CT is the best study
Subdural hematoma	Occurs in 1% after mild head injury; in chronic cases, up to 50% without history of head injury	Any age	Unilateral or bilateral	Mild to severe; may be aching, dull, or throbbing	Paroxysmal to constant	Normal neurologic exam in 50%; alteration in consciousness and focal findings may be present	MRI may detect the occasional isodense subdural hematoma, which can be missed on CT scan

CN V, Cranial nerve V; *CRP*, C-reactive protein; *CT*, computed tomography; *ESR*, erythrocyte sedimentation rate; *MRI*, magnetic resonance imaging; *PMR*, polymyalgia rheumatica; *STA*, superficial temporal artery; *WNL*, within normal limits.

Modified with permission from Evans RW: Diagnosis of headaches. In: Evans RW, Mathew NT, editors: Handbook of headache. 2nd ed. Philadelphia: Lippincott Williams & Wilkins, p. 1, 2005.

67. What are other common symptoms and test findings in SIH?
The headache can be associated with neck stiffness or pain, nausea ± vomiting, light and noise sensitivity, muffled hearing, tinnitus, interscapular pain, upper extremity radicular symptoms, sense of imbalance, and subtle cognitive dysfunction. Less commonly, patients report visual changes (blurring, visual field defects, diplopia), facial pain or numbness, facial weakness, and dysgeusia.

The MRI of the brain is abnormal in 80% of cases. The most common abnormality is diffuse pachymeningeal (dura and outer layer of the arachnoid mater) enhancement. The opening pressure on lumbar puncture will often be low, less than 60 mm of H_2O, but normal pressures are common. CSF may be clear or xanthochromic, with either normal or elevated protein (as high as 1000 mg/dL), normal glucose, and either a normal leukocyte count or a lymphocytic pleocytosis (as high as 222 cells/mm^2). The patient may also have an elevated erythrocyte count.

68. Other than low CSF volume syndrome such as PDPH or SIH, what are some other causes of orthostatic headaches?
Postural orthostatic tachycardia syndrome, after surgery for Chiari malformation, the syndrome of the trephined, increased compliance of the dural sac, and occasional cases of colloid cyst of the third ventricle.

69. What is the association between headaches and epilepsy?
Headaches and epilepsy are comorbid. The prevalence of migraine in epilepsy has ranged from 8% to 24% and of epilepsy in migraine from 1% to 17%. Headaches can occur in association with seizures as seizure-related or peri-ictal headaches. Pre-ictal headaches precede the seizure and occur in 5% to 15% of patients with epilepsy. Ictal headache is reported by less than 5% of patients with epilepsy. Post-ictal headache can occur immediately after a seizure and is reported in 10% to 50% of patients with epilepsy. The headaches can be migraine-like, tension-like, or unclassifiable. Migralepsy, referring to a seizure developing during or within 1 hour of a migraine aura, is extremely rare.

70. What is an ictal epileptic headache?
Ictal epileptic headache is a rare controversial disorder where a migrainous or tension-type headache is the sole manifestation of a seizure. Ictal epileptic headache has been reported in patients with focal seizures arising predominantly from the occipital lobes as well as with nonconvulsive status epilepticus and generalized idiopathic epilepsy.

71. What types of headaches are associated with Chiari I malformation?
Headache is the dominant feature associated with Chiari I malformation and is typically occipital with radiation to the vertex and retro-orbital or to the neck and shoulders. It is frequently triggered by physical activity, Valsalva, coughing, laughing, or change of body position, with a duration ranging from a few minutes to chronic. Most patients become symptomatic during the second or third decade of life, with a mean age of symptom onset of 24.9 ± 15.8 years.

72. What are the features of alcohol hangover headache (AHH)?
Alcohol hangover or "veisalgia" (from the Norwegian *kveis* for uneasiness following debauchery and the Greek *algia* for pain) may include physical symptoms (headache, anorexia, diarrhea, tremulousness, dizziness, fatigue, and nausea), sympathetic symptoms (tachycardia and sweating), and cognitive and mood symptoms (decreased attention and concentration, decreased visuospatial skills and dexterity, depression, anxiety, and irritability). AHH is typically a throbbing headache with a lifetime prevalence of 72%. The headache usually occurs on the morning after alcohol consumption when the blood alcohol concentration (BAC) is falling. Peak symptoms occur at about the time when the BAC is 0 and may continue for up to 24 hours afterward. Symptoms may correlate with the amount of alcohol consumed. Hangover is much more common in light to moderate drinkers than in regular heavy drinkers. Alcohol consumption may also trigger migraine and CH.

73. How can you decrease the risk of and treat AHH?
AHH occurs more often with dark-colored drinks with congeners (which are natural byproducts of alcohol fermentation) such as whiskey, bourbon, and red wine than in noncongeners such as vodka, gin, and white wine.

The effects of AHH may be decreased by the following: drinking in moderation; sipping beverages slowly; eating greasy foods before alcohol consumption to slow or delay alcohol absorption; ingestion of honey, tomato juice, and food rich in fructose, which may allow for more effective metabolism of alcohol; adequate sleep; not smoking; remaining hydrated with electrolyte-rich fluids to prevent dehydration; caffeine intake; and use of NSAIDs such as mefenamic acid for symptomatic treatment (but gastroduodenal risk).

74. What are high-altitude headaches (HAH)?
Acute ascent to an altitude above 2500 m can produce acute mountain sickness with a bilateral headache of mild or moderate intensity in up to 87%. It can be associated with nausea, photophobia, vertigo, poor concentration, and, in severe cases, impaired judgment. It resolves within 24 hours after descent to below 2500 m. High altitude is also a common migraine trigger.

75. How can HAH be treated and the risk reduced?
The risk of HAH can be reduced with the use of aspirin 320 mg taken three times at 4-hour intervals starting 1 hour before ascent or ibuprofen 600 mg three times a day starting 6 hours before ascent to an altitude between 3480 m and 4920 m; four doses total. Acetazolamide 125 mg every 12 hours starting 1 day prior to ascent and continued for 2 to 3 days at maximum altitude may also be effective. Slow ascent, copious fluid intake, avoidance of alcohol, and 2 days of acclimatization prior to strenuous exercise at high altitude may help to prevent HAH.

HAH can be treated with acetaminophen, ibuprofen, and antiemetics. Acetazolamide 125 to 250 mg bid or, as an alternative, dexamethasone 2 to 4 mg every 6 hours can be continued for 24 hours after symptoms either resolve or descent is complete. However, dexamethasone should be used for no longer than 7 days total.

76. What is sleep apnea headache?
Sleep apnea headache is a recurrent morning headache, which is usually a bilateral pressing pain without associated symptoms with a duration of less than 4 hours caused by sleep apnea (diagnosed by polysomnography) and which resolves with successful treatment of the sleep apnea.

77. What levels of hypertension are associated with headaches?
An often bilateral and pulsating headache may be associated with an acute rise in a systolic blood pressure to ≥180 mm Hg and/or diastolic to ≥120 mm Hg. It remits after normalization of blood pressure. Mild or moderate chronic hypertension does not appear to cause headache.

Hypertensive encephalopathy presents with persistent elevation of blood pressure to ≥180/120 mm Hg (typically in those with a history of chronic hypertension) and at least two of the following: confusion, reduced level of consciousness, visual disturbance including blindness, and seizures. Headache is reported at presentation in 22%. In those previously normotensive, encephalopathy may develop with blood pressure as low as 160/100 mm Hg. At increasing levels of blood pressures beyond the upper range of cerebral autoregulation, endothelial permeability increases and cerebral edema occurs, most prominently in the parieto-occipital white matter on MRI.

78. What other disorders can present with headaches and hypertension?
Severe frontal or occipital pulsating or constant paroxysmal headaches may occur in 51% to 80% of those with pheochromocytoma, variably accompanied by sweating, palpitations, pallor, anxiety, tremor, visual disturbances, abdominal or chest pain, nausea, vomiting, facial flushing, and occasionally paresthesias. The headaches typically last less than 1 hour in 70% of patients.

Preeclampsia and eclampsia occur during pregnancy or up to 4 weeks postpartum with a blood pressure of >140/90 mm Hg on two readings at least 4 hours apart or a rise in diastolic pressure of ≥15 mm Hg or of systolic pressure of ≥30 mm Hg along with urinary protein excretion greater than 0.3 g/24 hours. The usually bilateral and pulsating headache occurs in 63% of those with preeclampsia.

A severe throbbing headache can occur in 56% to 85% of those with a spinal cord injury (SCI) and autonomic dysreflexia. The headache of SCI and autonomic dysreflexia is associated with a paroxysmal rise above baseline in systolic pressure of ≥30 mm Hg and/or diastolic pressure ≥20 mm Hg and can be triggered by either noxious or nonnoxious stimuli such as bladder distention, urinary tract infection, bowel distention or impaction, gastric ulcer, decubiti, trauma, or procedures. The latency from onset after the SCI can range from 4 days to 15 years and is more common in those with a complete SCI.

79. Can hypothyroidism cause headaches?
About 30% of patients with hypothyroidism experience a typically bilateral nonpulsatile headache that resolves with treatment. Migraineurs with subclinical hypothyroidism may also improve with treatment. Hypothyroidism can also be a manifestation of a pituitary adenoma.

80. Can fasting cause headaches?
A generalized mild to moderate nonpulsating headache can occur during a fast of at least 8 hours and is relieved after eating (occurs in 47% after a 15-hour fast in one study). Fasting is a common trigger for migraineurs as reported by 57%.

81. What is cardiac cephalalgia?
Cardiac ischemia rarely may cause a unilateral or bilateral headache in any part of the head brought on by exercise and relieved by rest. This type of headache is called *cardiac cephalalgia* or *anginal headache*. Headaches may occur alone or be accompanied by chest pain. In cases of unstable angina, headaches may occur at rest. A thunderclap headache may accompany the chest pain.

82. What headaches are associated with temporomandibular disorders (TMDs)?
TMDs include musculoskeletal and neuromuscular conditions that involve the temporomandibular joints (TMJ), the masticatory muscles, and all associated tissues. A painful TMD may occur in 10% of the population. Other signs or symptoms of TMD such as clicking, limited range of motion, and pain on joint function have been reported in 46% of the US population.

The pain associated with TMD is frequently of muscular origin and the symptoms are often self-limiting. The pain is typically ipsilateral when arising from the TMJ or may be bilateral when muscular. The headache may be exacerbated by either jaw movement or pressure applied to the TMJ or surrounding musculature.

Sleep bruxism, which occurs in up to 31% of the population, may exacerbate TMD and/or headache symptoms, but a causal relationship is not evident.

Those with asymptomatic clicking often do not require treatment. Therapy is indicated if pain, signification limitation in mandibular range of motion, or both are present.

83. What are the features of classical trigeminal neuralgia (TN) due to neurovascular compression?
The annual incidence of TN is 4-13/100,000, with most cases starting after age 50 and a gradually increasing incidence with older age (although teens and young adults and rarely children may be affected). The male:female ratio is 1:1.7.

According to ICHD-3, the facial pain is unilateral with at least three of the following four characteristics: recurring in paroxysmal attacks lasting from a fraction of a second to 2 minutes; severe intensity; electric shock-like, shooting, stabbing, or sharp in quality; precipitated by innocuous stimuli to the affected side of the face. There is no clinically evident neurologic deficit.

TN is most commonly caused by compression of the nerve by the superior cerebellar artery. Imaging, preferably MRI, should be done, to exclude secondary causes such as multiple sclerosis (especially in patients under the age of 40 years), neoplasm, and basilar artery aneurysm.

84. What are the features of classical TN in a prospective series and what is pretrigeminal neuralgia?
In a prospective series of 158 patients, the average age of onset was 52.9 years, with 60% being females. TN affects the right side of the face in 56%, left side in 41%, and both sides in 3%. Pain was reported in the following distributions: V1, 4%; V2, 17%; V3, 19%; V1+V2, 10%; V2+V3, 33%; and V1+V2+V3, 13%. Thirteen percent had a more dull persistent pain at the onset of the disorder ("pretrigeminal neuralgia") while 87% had stabbing paroxysmal pain. The paroxysmal pain was rated on average 10/10 by 58% of the patients. Forty-nine percent of the cohort reported concomitant persistent pain along with the paroxysmal pain.

Forty percent suffered from more than 10 paroxysms of pain per day. Painful awakening at night because of pain attacks at least occasionally was reported by 49%. Trigger factors were reported by 91% included the following: chewing, 73%; touch, 69%; brushing teeth, 66%; eating, 59%; talking, 58%; and cold wind, 50%. During attacks of pain, 31% experienced ipsilateral autonomic symptoms, most commonly conjunctival tearing or injection. Of the surgery-naïve patients, 29% had sensory abnormalities on exam, most commonly hypesthesia confined to the painful area of the face. Most patients (63%) had periods of remission, with the average number per year of disease of 0.44 and 37% having months of remission and 63% experiencing years of remission.

85. What is the treatment of classical TN?
The most effective medication for TN is carbamazepine (200 to 2400 mg daily depending upon efficacy and tolerability), with efficacy in 58% to 100% of patients depending upon the study while oxcarbazepine (titrated up to 1800 mg daily depending upon effect and tolerability) is probably as effective as carbamazepine and may be effective in patients not responsive to carbamazepine. Baclofen (40 to 80 mg daily in three doses slowly titrated up) and lamotrigine (up to 400 mg daily slowly titrated up) are possibly effective while there are limited data on the benefit of other medications including clonazepam, phenytoin, tizanidine, topiramate, pregabalin, misoprostol, and valproate. Those who fail carbamazepine monotherapy may benefit from combination therapy with baclofen, gabapentin, tizanidine, lamotrigine, or topiramate. One trial found benefit from onabotulinumtoxinA. Acupuncture may be helpful.

Perhaps 40% of patients with TN do not respond to medication treatment. A joint society position paper of the American Academy of Neurology and the European Federation of Neurological Societies concluded that microvascular decompression, percutaneous procedures on the gasserian ganglion (rhizotomy), and gamma knife are possibly effective.

86. What is glossopharyngeal neuralgia?
Typically severe stabbing pain along one side of the throat near the tonsillar area with occasional radiation to the ear lasting fractions of a second up to 2 minutes is present, which can be precipitated by swallowing, coughing, talking, or yawning. Most patients are believed to have an artery compressing the nerve as it exits the medulla and travels through the subarachnoid space to the jugular foramen although secondary causes should be excluded by MRI and other testing (including tumors, multiple sclerosis, Paget's disease, Sjögren's syndrome, and other causes).

The incidence is about 0.2 to 0.7 per 100,000 patients, with most presenting older than 50 years of age and with a female:male ratio of 1:1. Medical treatment is the same as for TN. If intractable, surgical options include microvascular decompression and rhizotomy.

87. What are the features of persistent idiopathic facial pain (PIFP), formerly called atypical facial pain?
According to ICHD-3, the diagnostic criteria are the following: "A) Pain in the face, present daily and persisting for all or most of the day, fulfilling criteria B and C; B) Pain is confined at onset to a limited area on one side of the face, and is deep and poorly localized; C) Pain is not associated with sensory loss or other physical signs; D) Investigations including X-ray of face and jaws do not demonstrate any relevant abnormality."

"Note: Pain at onset is commonly in the nasolabial fold or side of the chin, and may spread to the upper or lower jaw or a wider area of the face and neck."

PIFP has a lifetime prevalence of perhaps 0.03% with a female:male ratio of 2:1.

88. What are secondary causes of PIFP and the treatment?
Secondary causes such as TMD, dental pathology, nasopharyngeal tumors, and rarely lung carcinoma should be excluded by evaluation by a dentist and appropriate testing including an MRI of the brain and radiologic examination of the chest.

Treatment is difficult. Amitriptyline, fluoxetine, venlafaxine, and topiramate may be effective.

89. What is occipital neuralgia?
Greater occipital neuralgia (GON) can be caused by trauma or be unrelated to trauma. It may be due to compression or irritation of the nerve by the muscles as the nerve passes through the semispinal capitis and trapezius. Although "true" GON is described as paroxysms of electrical pain in the distribution of the nerve, other patients can have longer duration pain. The pain can be referred in a suboccipital, hemicranial, temporal, frontal, orbital, periorbital, or retro-orbital distribution. Similarly, lesser occipital neuralgia can occur with pain referred in the distribution of the nerve over the lateral scalp superior and posterior to the ear and sometimes in the ear. On examination, there is tenderness over the involved nerve with reproduction of symptoms. There may be hyperesthesia, dysesthesia, or paresthesia in the involved scalp.

Primary and secondary headaches including temporal arteritis can mimic occipital neuralgia so diagnostic testing may be indicated. Occipital nerve block with local anesthetic can be quite effective (but can also be effective for migraine). Other treatments may include physical therapy, NSAIDs, baclofen, carbamazepine, gabapentin, pregabalin, and tricyclic antidepressants.

KEY POINTS: HEADACHES

1. Ninety percent of headaches are primary, and 90% of headaches seen by primary care physicians are migraine.
2. Most headaches are diagnosed by the history and physical examination where diagnostic testing is not indicated.
3. Consider the risk of medication overuse when treating migraineurs with frequent headaches.
4. Consider subarachnoid hemorrhage as the cause of thunderclap headaches or worse headaches. Temporal arteritis should be considered as the cause of new-onset headaches in those over the age of 50 years.

References available online at expertconsult.com.

WEBSITES

http://www.americanheadachesociety.org/
http://www.ihs-headache.org/

BIBLIOGRAPHY

1. Evans RW (ed): Secondary headache. Neurol Clin 32(2):283-568, 2014.
2. Evans RW (ed): Migraine and other primary headaches. Neurol Clin 27(2):321-582, 2009.
3. Headache Classification Committee of the International Headache Society (IHS): The International Classification of Headache Disorders, 3rd ed (beta version). Cephalalgia 33(9):629-808, 2013.
4. Loder E, Weizenbaum E, Frishberg B, et al.: Choosing wisely in headache medicine: the American Headache Society's list of five things physicians and patients should question. Headache 53:1651-1659, 2013.