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RELATIONSHIP DISCLOSURE:
Dr Gelfand has received personal compensation for serving on the medical advisory board of eNeura Inc; as associate editor for *JAMA Neurology;* and as a consultant for Biohaven Pharmaceutical, Eli Lilly and Company, and Zosano Pharma Corporation.
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UNLABELED USE OF PRODUCTS/INVESTIGATIONAL USE DISCLOSURE:
Dr Gelfand discusses the unlabeled/investigational use of all listed medications for the treatment of headache in children and adolescents, with the exceptions of almotriptan oral tablets, sumatriptan/naproxen combination tablets, and zolmitriptan nasal spray for adolescents 12 to 17 years of age for the treatment of acute migraine as well as topiramate in adolescents 12 to 17 years of age for migraine prevention. Rizatriptan is labeled for acute migraine treatment in children age 6 and older.

Pediatric and Adolescent Headache

By Amy A. Gelfand, MD

ABSTRACT

PURPOSE OF REVIEW: This article provides the practicing neurologist with a comprehensive, evidence-based approach to the diagnosis and management of headache in children and adolescents, with a focus on migraine.

RECENT FINDINGS: Four triptans are now labeled by the US Food and Drug Administration (FDA) for acute migraine treatment in adolescents, and rizatriptan is labeled for use in children age 6 and older. For preventive migraine treatment, the Childhood and Adolescent Migraine Prevention trial demonstrated that approximately 60% of children and adolescents with migraine will improve with a three-pronged treatment approach that includes: (1) lifestyle management counseling (on sleep, exercise, hydration, caffeine, and avoidance of meal skipping); (2) optimally dosed acute therapy, specifically nonsteroidal anti-inflammatory drugs and triptans; and (3) a preventive treatment that has some evidence for efficacy. For the remaining 40% of children and adolescents, and for those who would not have qualified for the Childhood and Adolescent Migraine Prevention trial because of having continuous headache or medication-overuse headache, the clinician's judgment remains the best guide to preventive therapy selection.

SUMMARY: Randomized placebo-controlled trials have been conducted to guide first-line acute and preventive migraine treatments in children and adolescents. Future research is needed to guide treatment for those with more refractory migraine, as well as for children and adolescents who have other primary headache disorders.

INTRODUCTION

Headache is one of the most common neurologic symptoms that brings a child or adolescent to the neurologist's office. The clinician's first task is to separate those few children who have a dangerous underlying secondary cause of headache from the majority who have a primary headache disorder such as migraine. A thorough history and neurologic examination are usually the only tests needed to make this distinction, although in some instances neuroimaging, CSF examination, EEG, or other tests may be needed. This article aims to help practicing neurologists develop an approach to pediatric

headache history taking, identify red flags for secondary headaches in children, recognize diagnostic features of primary headache disorders in this age group, and recommend evidence-based treatment strategies.

APPROACH TO PEDIATRIC HEADACHE HISTORY TAKING

Children are remarkably good headache historians. Having a planned, systematic approach to pediatric headache history taking is essential. One advantage in pediatric headache history taking is that a parent/guardian will almost always be in the room. The parent/guardian can provide detailed information about the child's birth and development, the presence or absence of early episodic syndromes that may be associated with migraine,[1] and any family history of migraine (which is helpful as migraine often occurs in those with a family history). There may also be an opportunity to take a direct headache history from a first-degree relative when the parent/guardian is biologically related to the child. Parents may not recognize that their "normal headaches" are, in fact, migraine. For example, a woman who develops pounding headaches each month before her menses and must lie down in a dark room may only learn that she has migraine when she attends her child's neurology visit. Only 48% of adults with migraine in the United States have ever received a migraine diagnosis by a physician,[2] so it would not be surprising to uncover a parent with undiagnosed migraine.

Having a parent/guardian in the room during history taking can also be a challenge. In his or her desire to help the child, the parent/guardian may be inclined to try to provide the child's headache history themselves. Below are suggested strategies for facilitating pediatric headache history taking (in neurodevelopmentally typical children).

Step 1: Assign Seats

Have the child or adolescent sit closest to the clinician. The parent/guardian can sit to the side of his or her child. This seating arrangement sends the message that the patient is the focus of the visit. The parent/guardian is there to help and support, not to take over.

Step 2: Set Expectations at the Outset

Introducing the headache history taking process at the outset of the visit can help to set everyone's expectations. While making eye contact with the child or adolescent, the clinician can say something to the effect of, "I am going to ask you a number of questions about your headaches. I tend to ask my questions to you, because it's your head, and you know best. However, if there's anything you're not sure about, feel free to ask your [parent/guardian(s)] for help. I'm sure they'd be happy to help you out. At the end, if there's anything I missed that you think is important, I'll give you an opportunity to add it in, and your [parent/guardian(s)] will have an opportunity as well."

This brief speech sets up the expectation that the history taking is going to predominantly be a conversation between the clinician and the child or adolescent, but that there will be an opportunity for the parent/guardian(s) to add in his or her important perspective. It also reassures the child that if he or she cannot remember something or is not sure about something, the parent/guardian is right there to offer support.

Step 3: Take the Headache History

The history taking can then generally proceed as it would with an adult. As the headache neurologist Peter J. Goadsby, MD, PhD, is fond of saying, "Good headache histories are taken, not given." Having a systematic, structured approach to headache history taking will allow the clinician to come to a clear diagnosis. Some age-specific points are included below.

VERY YOUNG CHILDREN. Children younger than age 6 may have difficulty providing the details of their headache history. In this age group, parents/guardians likely will need to provide a fairly large proportion of the history. Having children draw a picture of themselves and how they feel during a headache can be diagnostically helpful.[3] The tissue paper on the examining table can be a ready source of drawing paper for impromptu art production.

PREADOLESCENT SCHOOL-AGED CHILDREN. Time can be a challenging concept for this age group, hence details such as duration and frequency (ie, How long do the headaches last? How many times a week or a month do they happen?) may still need to come from the parent/guardian. Medication names and dosages likely also will come from the adult caregiver.

ADOLESCENTS. Adolescence spans a tremendous developmental range. Some children at 12 years of age will be able to give their entire history, right down to their sumatriptan dose, while others at 17 years of age will still be shrugging and looking to their parents. As a generality, however, adolescents can give a complete headache history, and parental assistance will likely be minimal. It is acceptable to ask the parent/guardian to step out of the room for a few moments to allow for a confidential discussion with the teen around sensitive issues such as alcohol and drug use.

RED FLAGS FOR SECONDARY HEADACHE PATHOLOGY IN CHILDREN AND ADOLESCENTS

This section focuses on features to watch out for in the child or adolescent who experiences recurrent headaches at home and presents to the neurology clinic for outpatient evaluation. "First or worst" headaches (eg, the singular thunderclap headache that occurs with subarachnoid hemorrhage) are more likely to present in the emergency department. Red flags for secondary headache pathology in children and adolescents tend to overlap with secondary headache evaluation in adults, with the exception of select epidemiologic diagnostic considerations in older adults and some pediatric-specific nuances. For more information, refer to the article "Secondary Headache Syndromes" by Denise E. Chou, MD,[4] in this issue of *Continuum*.

Headaches Occurring When Supine or With Valsalva Maneuver

While children with migraine might occasionally have a headache that wakes them from sleep at night, a regular pattern of headaches occurring at night while supine or occurring exclusively with Valsalva maneuver or cough suggests elevated intracranial pressure and the possibility of a mass, which warrants further investigation.

Headaches With Exercise, Sexual Activity, or Cough

While primary headache disorders may occur with exercise, sexual activity, or cough,[1] they are diagnoses of exclusion, and generally neuroimaging is needed to exclude secondary causes of these types of headaches.

KEY POINT

● New headaches, or new types of headaches, are more concerning for secondary pathology than old headaches.

Recurrent Thunderclap Headaches

Thunderclap headaches (ie, those that come on suddenly and are maximal in intensity at onset) occurring in a flurry of attacks over the course of a few days or weeks can suggest reversible cerebral vasoconstriction syndrome (RCVS).[1]

New-onset Headaches With Accompanying Concerning Features

New-onset headaches with accompanying features suggestive of meningitis, encephalitis, or a focal neurologic process (eg, seizure, movement disorder, altered mental status) or signs of systemic illness or infection) require further evaluation.

Visual Symptoms not Characteristic of Migraine Aura

Focal childhood epilepsy syndromes can mimic migraine with visual aura. Panayiotopoulos syndrome is an epilepsy syndrome with a peak age of onset of 3 to 6 years. The child may describe colored spinning balls or other visual hallucinations.[5] In contrast, visual symptoms in migraine aura are usually "negative" (eg, scotomata or the black and white jagged curvilinear outline of a fortification spectrum).[1] Autonomic symptoms such as nausea, vomiting, and pallor are typical in Panayiotopoulos syndrome. Autonomic seizures can last for 30 minutes or more and may end with altered consciousness, nystagmus, and convulsion. The total number of seizures in Panayiotopoulos syndrome is low, and patients typically have fewer than five lifetime seizures from Panayiotopoulos syndrome. A second epilepsy syndrome, idiopathic childhood occipital epilepsy of Gastaut, usually starts around 8 to 11 years of age. Children may describe colored spinning objects or visual hallucinations/illusions followed by severe headache and sometimes vomiting. Visual episodes are stereotyped, coming on within seconds and typically lasting just a couple of minutes.[5] By contrast, visual aura in migraine typically develops slowly over minutes and lasts for at least 5 minutes.[1] The occipital lobe seizures in Gastaut epilepsy are typically frequent and brief.[5] Usually, the clinical description is enough to reassure the clinician that the child does not have epilepsy, but if question remains, an EEG is indicated.

Headaches Worsening When Upright

Headaches that worsen with standing may suggest spontaneous intracranial hypotension or post–dural puncture headache if a recent lumbar puncture has occured.[1]

Headaches Accompanied by Diplopia, Transient Visual Obscurations, Decreased Visual Acuity, or Visual Field Deficits

Headaches accompanied by diplopia, transient visual obscurations, decreased visual acuity, or visual field deficits are suggestive of intracranial hypertension, including idiopathic intracranial hypertension (pseudotumor cerebri). Children on medications known to cause this disorder or adolescent females with an elevated body mass index are most likely to be affected. Note that an opening pressure of 280 mm CSF or more is needed to make this

diagnosis in children who are obese or sedated, compared to 250 mm CSF or more in adults or in children who are not obese or sedated.[6]

Brief Side-locked or Site-locked Headaches Associated With Symptoms of Endocrine Pathology

Functional or structural pituitary lesions can generate secondary headaches that are brief and sometimes phenotypically mimic trigeminal autonomic cephalalgias.[7] Abnormalities of growth, galactorrhea, or symptoms of hypothyroidism/hyperthyroidism can be suggestive of pituitary pathology. Trigeminal autonomic cephalalgias are side-locked and site-locked headaches; however, these disorders are rare in children, so before finalizing such a diagnosis, an MRI of the brain, with special attention to the pituitary, should be obtained.

Focal Neurologic Examination Findings

On initial presentation for headache, all children and adolescents need a thorough neurologic examination including funduscopic examination. Focal findings, unless long-standing and previously explained (eg, a well-documented right hemiparesis from a known left middle cerebral artery perinatal stroke), require neuroimaging.

Immunocompromised Child or Adolescent

Children with a history of cancer, immunosuppressive therapy, a congenital or acquired immunodeficiency, or on anticoagulation will likely need neuroimaging to exclude secondary pathology before finalizing a primary headache diagnosis, even in otherwise typical headache syndromes.

PEDIATRIC HEADACHE FEATURES NOT RED FLAGS FOR SECONDARY PATHOLOGY

Recognizing headache features that are common in children can help to avoid unnecessary testing.

Occipital Headache Location

In the emergency department setting, occipital headache in children has been associated with brain tumors.[8,9] However, the children with tumors in those studies also had objectively abnormal neurologic examinations. In the clinic setting, the child who has recurrent occipital headaches but a normal neurologic examination and headaches that are otherwise consistent with migraine does not appear to be at increased risk of secondary pathology.[10] Occipital headache alone is not necessarily a reason to image.

Headaches Accompanied by Nasal Congestion, Itchy Eyes, or Ear Pressure

"Sinus headache" is one of the most common misdiagnoses given to adult and pediatric patients who have migraine.[11,12] This misdiagnosis can result in unnecessary courses of antibiotics, unnecessary sinus surgeries, and delays in diagnosis and appropriate treatment of migraine. Cranial autonomic symptoms are common in pediatric migraine; in fact, the majority of patients will have at least one cranial autonomic symptom (FIGURE 8-1),[13,14] and their presence should not dissuade the clinician from making a diagnosis of migraine. These symptoms result from activation of trigeminal nociceptive afferents and parasympathetic efferent outflow in cranial nerves VII and

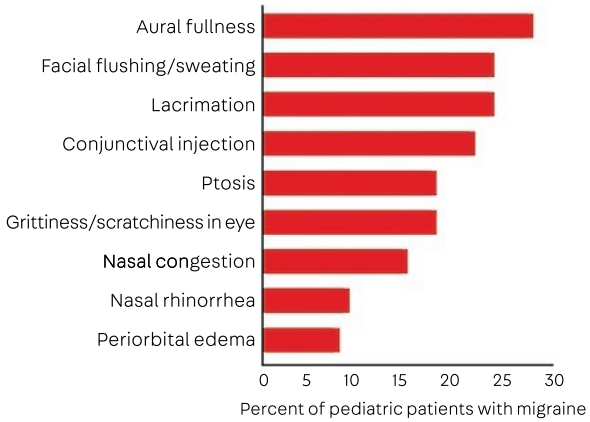

FIGURE 8-1
Frequency of cranial autonomic symptoms in patients with pediatric migraine.
Reprinted with permission from Gelfand AA, et al, Neurology.[13] © 2013 American Academy of Neurology.

VIII.[15] The list of cranial autonomic symptoms recognized in the *International Classification of Headache Disorders, Third Edition* (*ICHD-3*) is as follows[1]:

- **Conjunctival injection and/or lacrimation**
- **Nasal congestion and/or rhinorrhea**
- **Eyelid edema**
- **Forehead and facial sweating**
- **Forehead and facial flushing**
- **Sensation of fullness in the ear**
- **Miosis and/or ptosis**

PRIMARY HEADACHE DISORDERS AFFECTING CHILDREN AND ADOLESCENTS

Many different primary headache disorders can affect children and adolescents.

Migraine

While sometimes thought of as an adult disorder, migraine can occur in children and adolescents.

EPIDEMIOLOGY, DIAGNOSIS, AND IMPACT. Migraine is common in children and adolescents. By age 10, the prevalence of migraine in children is approximately 5%, and it increases further over the course of adolescence (FIGURE 8-2).[16] Prior to puberty, migraine affects boys and girls equally.[16] By late adolescence, migraine affects more girls than boys, ultimately approximating the 3:1 ratio seen in adult women and men.[16,17] (Refer to the open access online version of the *ICHD-3* for a complete listing of the diagnostic criteria of migraine in children and adolescents.[1])

Chronic migraine, referring to headache occurring 15 days or more per month for 3 months or more, of which 8 or more meet criteria for migraine,[1] is also common in children and adolescents. Among children ages 5 to 12 years,

KEY POINT

- **By age 10, migraine prevalence in children is approximately 5%. This means that by fifth grade, almost every classroom contains at least one child with migraine.**

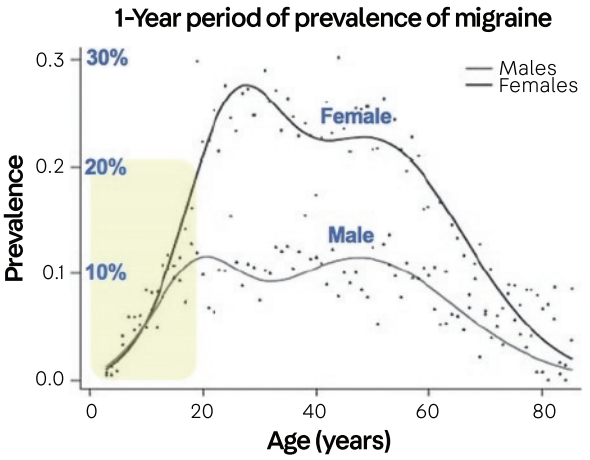

FIGURE 8-2
Migraine prevalence by age and sex.
Modified with permission from Victor TW, et al, Cephalalgia.[16]

chronic migraine prevalence is 0.6%.[18] In adolescents 12 to 17 years of age, the prevalence of chronic migraine is 0.8% to 1.8%.[19] Children from socioeconomically disadvantaged backgrounds are 4 times more likely to experience chronic migraine.[18]

Children with migraine miss more school and perform more poorly in school than their headache-free peers. A dose effect occurs, wherein children with chronic migraine tend to miss more school than those with episodic migraine.[18] In the recent Childhood and Adolescent Migraine Prevention (CHAMP) trial, a National Institutes of Health (NIH)–funded multisite migraine prevention study for participants ages 8 to 17 years, the 361 participants missed 165 full days of school and 124 partial days of school during the 4-week run-in period alone.[20] In children with migraine, nausea during migraine attacks is the strongest predictor of missing school (odds ratio of 5.7; 95% confidence interval, 2.6-12.4).[18] Migraine has a tremendous capacity to cause disability and to negatively impact a child's schooling.

Measuring and quantifying migraine-associated disability in children and adolescents is important for determining the appropriate level of treatment intervention and for following treatment response over time. The Pediatric Migraine Disability Assessment (PedMIDAS) questionnaire is a six-question validated instrument for measuring headache-related disability in children and adolescents.[21] A version can be downloaded for free at *cincinnatichildrens.org/service/h/headache-center/pedmidas*.[22]

PHENOTYPE OF MIGRAINE IN CHILDREN. As in adults, children and adolescents with migraine can experience premonitory symptoms and postdrome symptoms in addition to ictal phase symptoms of migraine,[23] although the most common symptoms experienced by these age groups may differ from adults. Premonitory symptoms precede the headache phase of migraine by hours or even a day or two and include symptoms such as neck pain, mood change, food cravings, photophobia/phonophobia, and increased yawning. Postdrome symptoms follow the headache phase and include fatigue, a "washed out" feeling, and brain fog. (Refer to the articles "The Migraine Premonitory Phase" and "The Migraine Postdrome" by Nazia Karsan, MBBS, MRCP; Pyari Bose, MD, MRCP; and Peter J. Goadsby, MD, PhD,[24,25] in this issue of *Continuum*.) Symptoms in the premonitory and postdrome phase scan impact function and contribute to migraine-related disability.

PREMONITORY PHASE OF PEDIATRIC AND ADOLESCENT MIGRAINE. Premonitory symptoms are seen in approximately two-thirds of children and adolescents with migraine.[23] Fatigue, irritability/mood change, neck stiffness, and facial changes are the most commonly reported premonitory symptoms in this age group.[23,26]

MIGRAINE TRIGGERS VERSUS PREMONITORY SYMPTOMS. Patients can sometimes misinterpret a premonitory symptom as a migraine trigger. For example, if the brain has already entered the premonitory phase and become excessively sensitive to light, the person might erroneously conclude that bright lights triggered the headache. Importantly, in a randomized double-blind trial, chocolate was no more likely to trigger a migraine attack than was the control substance.[27] This was true regardless of whether the person thought chocolate was a trigger for them. Food craving, often for sweet foods, is a known premonitory phase migraine symptom, hence migraine may cause chocolate eating rather than chocolate causing migraine.

ICTAL PHASE OF PEDIATRIC AND ADOLESCENT MIGRAINE. The pathophysiology of migraine in children is likely similar to that in adults. Calcitonin gene-related peptide (CGRP) levels are elevated in pediatric migraine attacks just as they are in adult migraine attacks (FIGURE 8-3).[28] However, the phenotype of migraine in the developing brain has some unique features.

PHENOTYPIC FEATURES OF MIGRAINE THAT DIFFER IN CHILDREN AND ADOLESCENTS VERSUS ADULTS. Migraine duration in children can be shorter, particularly in children younger than 7 years of age.[29] In the *ICHD-3*, the lower margin of duration for untreated or unsuccessfully treated attacks in children is 2 hours versus 4 hours in adults.[1] It is not known why migraine tends to be shorter in the developing brain; however, one possibility might be that younger children are more likely to take naps, and sleep seems to be helpful in terminating migraine attacks.[29] The majority (more than 80%) of children and adolescents report bilateral migraine headache. This is the phenotype through late adolescence.[30]

EPISODIC SYNDROMES THAT MAY BE ASSOCIATED WITH MIGRAINE. Previously referred to as childhood periodic syndromes, certain disorders that tend to affect young children more often than adults have been associated with migraine and may represent early life manifestations of migraine genes in the

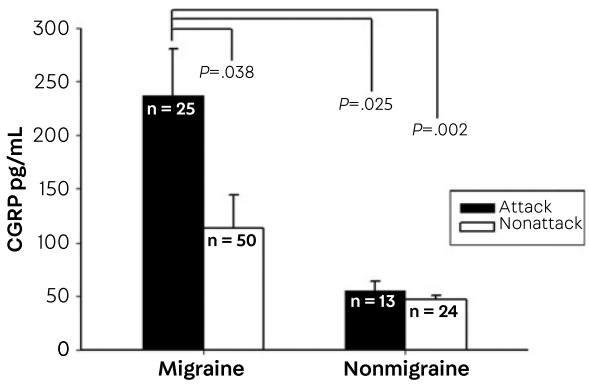

FIGURE 8-3
Calcitonin gene-related peptide (CGRP) levels in children with migraine versus children with nonmigraine headache both during headache and when without headache.
Reprinted with permission from Fan PC, et al, Cephalalgia.[28]

KEY POINTS

- **The Pediatric Migraine Disability Assessment questionnaire is a six-question validated instrument for measuring headache-related disability in children and adolescents.**
- **Common premonitory symptoms in pediatric migraine include fatigue, irritability/mood changes, neck stiffness, and facial change.**
- **Differentiating premonitory symptom from migraine triggers can be challenging.**
- **Chocolate does not appear to be a migraine trigger.**

developing brain. These include infant colic, benign paroxysmal torticollis, benign paroxysmal vertigo, cyclic vomiting syndrome, and abdominal migraine.[1]

INFANT COLIC. Excessive crying in an otherwise healthy and well-fed infant (infant colic) affects 5% to 19% of babies. While all babies cry, these babies cry more and often inconsolably. Children with migraine are more likely to have been colicky as babies,[31,32] women with migraine are more likely to have a baby with colic,[33] and babies with colic are more likely to grow up to have migraine without aura as adolescents.[34] It has been hypothesized that babies with migraine genetics may be more sensitive to stimuli than other babies, and that they express this sensitivity to stimuli through excessive crying at the end of the day.[33] Data suggest that colicky babies are more sensitive to sound and smell and cry most in the evenings and at night.[35] Excessive crying is associated with caregiver frustration and shaken baby syndrome[36,37]; hence, it is important that colic's etiology is ultimately understood so that these infants can be managed appropriately.

BENIGN PAROXYSMAL TORTICOLLIS. Starting in infancy, children with benign paroxysmal torticollis experience periodic attacks of head tilt, nausea/vomiting, and fussiness. For those children old enough to crawl or walk, ataxia may also be present. Some children have accompanying gross motor delay, which may be secondary to the effects of torticollis and ataxia that decrease the amount of time the child has to develop gross motor skills.[38] The calcium channel gene mutation *CACNA1A*, one of the genes associated with familial hemiplegic migraine, has been found in some individuals with benign paroxysmal torticollis.[39] Benign paroxysmal torticollis is rare, and referral to child neurology for diagnostic confirmation and treatment is recommended.

BENIGN PAROXYSMAL VERTIGO. Starting around preschool age, children with benign paroxysmal vertigo experience periodic attacks of dizziness typically lasting for several minutes. They may drop to the floor and have nystagmus. Epilepsy is on the differential. The natural history is to outgrow the episodes after several years.[40]

CYCLIC VOMITING SYNDROME. Cyclic vomiting syndrome typically occurs in elementary school–aged children and presents as periodic attacks of frequent vomiting. Accompanying abdominal discomfort and anorexia may be present. Inborn errors of metabolism can mimic this phenotype and should be considered in children who have developmental delay or regression, encephalopathy with attacks, or attacks clearly triggered by fasting or illness.[41] Adolescents with a cyclic vomiting phenotype should be asked about cannabis use and whether they take long showers or bathe in hot water during vomiting attacks, as cannabinoid hyperemesis syndrome is a diagnostic mimic.[42] Adults can also have cyclic vomiting syndrome. Antiemetics, triptans, and the neurokinin-1 receptor antagonist aprepitant[43] may be helpful in treating this disorder. L-carnitine and coenzyme Q10 supplementation may also be helpful.[41]

ABDOMINAL MIGRAINE. School-age children with abdominal migraine have periodic attacks of abdominal pain that is dull or "just sore" in quality. It tends

to be diffuse in location, and this feature is helpful in distinguishing it from abdominal pathology that tends to have localized pain. Associated pallor, anorexia, nausea, and vomiting may be present. Adults can also have abdominal migraine. Antiemetics, triptans, and dihydroergotamine may be helpful in treating this disorder.[44]

KEY POINT

● Cannabinoid hyperemesis syndrome can mimic cyclic vomiting syndrome in adolescents.

POSTDROME PHASE OF PEDIATRIC AND ADOLESCENT MIGRAINE. In one study, 82% of children and adolescents experienced postdrome symptoms. The most common symptoms were thirst, somnolence, visual disturbances, and food cravings.[45] In the vast majority of patients, postdrome symptoms resolved within 12 hours. Additional research in this area is needed. One advantage to migraine preventive treatment is that acute treatments focus on treating ictal phase symptoms and do not necessarily avoid the premonitory or postdromal symptoms and their associated disability. Preventing the attack entirely is optimal for minimizing disability.

TREATMENT OF PEDIATRIC AND ADOLESCENT MIGRAINE

Migraine treatment consists of two broad categories: preventive treatments (ie, things done to attempt to decrease migraine frequency) and acute treatment (ie, things done to attempt to decrease or stop acute symptoms).

Lifestyle Aspects of Migraine Prevention

Maintaining regularity and homeostasis is generally helpful in individuals with migraine. However, change is the rule in childhood and adolescence, and thus adolescence can be a challenging time for controlling migraine frequency. Physical, cognitive, and emotional growth are ongoing. Changes in schedule are near ever-present in this age group. While children with migraine are sometimes accused of "faking" a headache to get out of school, empirically they are no more likely to present to the emergency department for headache during a school month than a summer month.[46] The only exceptions are that (in the Northern Hemisphere) adolescents are more likely to present in September and January—the 2 months of the year when they go through significant changes in sleep and activity schedules as they transition from holiday schedules back to school. It therefore seems to be "changes in daily schedules and transitions" that are related to migraine frequency, rather than school itself.[46]

Several areas related to lifestyle regularity are worth discussing with children and adolescents and their families. In the CHAMP study, counseling around lifestyle aspects of migraine management was done at each month's study visit, which may have contributed to the excellent response seen in approximately 60% of the placebo arm.[47]

SLEEP. An optimal sleep schedule for a child or adolescent with migraine is one that includes adequate sleep (TABLE 8-1[48]) and bedtime and wake-up times that do not differ significantly from weekday to weekend. Achieving these goals can be particularly difficult for adolescents. Adolescents have a physiologic sleep phase delay wherein their brains do not want to go to sleep until later at night and want to sleep in.[49] High school schedules rarely accommodate adolescent neurobiology. While the American Academy of Pediatrics recommends that high schools begin no earlier than 8:30 AM,[50] only

17.7% of schools actually do.[51] Adolescents often sleep little during the week and try to make up for it over the weekend. Difficulty falling asleep Sunday night before the school week begins or inadequate sleep Sunday night may contribute to Monday being the most migrainous day of the week.[52] Clinicians can advocate for appropriate school start times with their local school districts. Consider excusing patients from their first period classes if it is necessary for improving migraine management.

HYDRATION. Increasing water intake is associated with improved headache severity and quality of life measures in adults with headaches.[53,54] In one study, 55% of all children and adolescents 6 to 19 years of age were mildly dehydrated based on tests of urine concentration.[55] *Headachereliefguide.com* is a website developed by pediatric headache experts that gives patients and families information about migraine in children and adolescents.[56] Children can go to the site to determine their individual water needs based on their sex, weight, the weather, and their level of physical activity for the day.

CAFFEINE. Caffeine withdrawal can provoke migraine. The clinician can determine whether the adolescent should avoid caffeine entirely or maintain a regular, modest, age-appropriate intake.

AVOIDING MEAL SKIPPING. Fasting can provoke headache.[57,58] For adolescents with migraine, the issue is usually inadequate time in the morning to eat breakfast (see above on start times for high schools). Portable breakfasts such as fruit and cheese can help.

EXERCISE. In an adult study where individuals with migraine were randomly assigned to either topiramate or aerobic exercise for 40 minutes (15 minute warm-up, 20 minute exercise, 5 minute cooldown) 3 times per week, both groups improved equally.[59] Prescribing exercise to a child seems generally healthier than prescribing topiramate, so it is worth spending some time discussing strategies for the child to get adequate physical activity.

TABLE 8-1

American Academy of Sleep Medicine Recommendations for Sleep in Children and Adolescents[a]

Age of Children/Adolescents	Recommended Hours of Sleep
3–5 years of age	10–13 hours of sleep per 24 hours (including naps)
6–12 years of age	9–12 hours of sleep per 24 hours
13–18 years of age	8–10 hours of sleep per 24 hours

[a] Data from Paruthi S, et al, J Clin Sleep Med.[48]

Behavioral Preventive Treatments for Pediatric and Adolescent Migraine

Cognitive-behavioral therapy, in combination with preventive medication, has been shown to help adolescents with chronic migraine in the 10 to 17 year age group improve more than medication plus lifestyle advice.[60] The course of therapy needed to provide benefit may be relatively short. Improved adherence may be part of the mechanism by which cognitive-behavioral therapy improves migraine frequency. For example, while it is one thing for the doctor to say, "keep a regular sleep schedule," it is another thing entirely for the adolescent and family to actually apply that advice. Coming up with strategies to facilitate regular sleep and good sleep hygiene is just one example of the type of skill building that can be achieved as part of cognitive-behavioral therapy. However, accessing cognitive-behavioral therapy can be challenging for patients and families.

Examples of barriers to accessing cognitive-behavioral therapy include stigma around anything called "therapy," inadequate insurance coverage for biobehavioral services, and inadequate numbers of providers trained in cognitive-behavioral therapy for headache in children and adolescents.

Overcoming barriers to cognitive-behavioral therapy is important.[61] Families can call their insurance company or third-party payer for a list of in-network providers in their area. The primary care pediatrician or family practice provider may have a list of appropriate providers in the family's area. Ultimately, technology-based solutions will likely be needed to fill the accessibility gap, such as telemedicine and cognitive-behavioral therapy smartphone apps. Several online programs already exist for cognitive-behavioral therapy for insomnia.

Pharmacologic Preventive Treatment

The CHAMP trial published in 2017 has helped to reframe the approach to migraine prevention in children and adolescents.[47] In this NIH-funded multisite trial designed to identify a first-line preventive for pediatric migraine prevention in children and adolescents ages 8 to 17 years, participants could have episodic or chronic migraine, although approximately three-fourths of the participants had episodic migraine.[20] A PedMIDAS score of 10 or more was an inclusion criterion in CHAMP, as this was thought to be the minimum amount of disability at which a pharmacologic preventive would be indicated.

The three treatment arms of the CHAMP trial were amitriptyline (goal dose of 1 mg/kg), topiramate (2 mg/kg), and placebo. During the course of the CHAMP study, topiramate became the first migraine preventive to be labeled by the US Food and Drug Administration (FDA) for migraine prevention in adolescents 12 to 17 years of age, based upon an earlier study of topiramate in this age group.[62]

The CHAMP trial was ultimately stopped early for futility. In all three treatment arms, approximately 60% of the participants met the primary end point of a 50% or more reduction in headache days 24 weeks after starting preventive therapy.[47] Adverse events were more commonly seen in the amitriptyline and topiramate arms than in the placebo group. Topiramate currently remains FDA-labeled for migraine prevention in adolescents 12 to 17 years of age, and no preventive therapies labeled for children younger than age 12 exist.

KEY POINTS

- **Combine cognitive-behavioral therapy with pharmacologic preventive treatment for chronic migraine in children and adolescents ages 10 to 17 years.**
- **First-line pharmacologic preventives for pediatric and adolescent migraine should have a side effect profile comparable to that of placebo.**
- **In the United States, 504 plans allow children and teenagers to have necessary accommodations at school for management of a medical condition, such as migraine. All children and adolescents with migraine should have an annual letter from their doctor stating their diagnosis and supporting accommodations for their 504 plan.**

Several factors may have contributed to the high placebo response rate seen in the CHAMP trial.[63] One is the possibility of active cointerventions. In addition to pharmacologic prevention, all participants received:

- **Lifestyle migraine management advice on sleep, exercise, hydration/eating, and caffeine. This advice was reinforced at monthly study visits. Attending to these aspects of prevention may have contributed to participants doing well.**
- **Optimal acute therapy: All participants received evidence-based optimal acute therapy, specifically nonsteroidal anti-inflammatory drugs (NSAIDs) and triptans, dosed appropriately and with use frequency guidance so as to avoid medication overuse. In adults, inadequate acute treatment efficacy is associated with an increased risk of progressing from episodic to chronic migraine.[64] Thus, optimizing treatment of acute attacks may itself have a preventive role.**

Of note, however, these interventions alone were not enough to decrease headache frequency, at least over the 4-week baseline run-in period. Participants' odds of having a headache in the fourth week of the run-in period were no lower than in the first week of the run-in period.[20] It seems that providing a preventive treatment was essential for bringing about headache frequency reduction. As treatment efficacy in the three arms was comparable, but adverse events were higher in the medication arms, these data suggest that first-line preventive treatments for pediatric migraine should have a side effect profile that is comparable to that of placebo.[63]

Preventive treatments with preferable side effect profiles include:

- **Melatonin 3 mg nightly: In an adult randomized placebo-controlled trial of melatonin 3 mg versus amitriptyline 25 mg versus placebo for migraine prevention, melatonin was more effective than placebo and similar in effect to amitriptyline. Melatonin had a side effect profile similar to placebo and better than amitriptyline.[65]**
- **Riboflavin 400 mg/d: In an adult randomized placebo-controlled trial of riboflavin versus placebo, riboflavin was superior to placebo and had excellent tolerability.[66]**
- **Cognitive-behavioral therapy: Evidence of efficacy has been shown,[60] and side effects would be expected to be minimal, although time and cost are considerations, and accessibility may be an issue.**
- **Low-dose prescription medications: For example, amitriptyline 10 mg nightly may have a favorable side effect profile, and there is some[67] evidence in adults for migraine preventive efficacy at low doses.**

The treatments suggested may help the approximately 60% of children and adolescents with migraine who would have met CHAMP inclusion criteria.

However, two important populations of patients remain: the approximately 40% of CHAMP-eligible children and adolescents with migraine who do not respond to first-line therapy, and those who would not have qualified for CHAMP (TABLE 8-2[68]) and to whom its results therefore do not necessarily generalize.

It has been observed that the children and adolescents most in need of effective migraine prevention (ie, those with continuous headache, high levels of migraine-related disability, or medication overuse) were the very ones excluded from CHAMP.[63]

In managing these two populations of patients, we still do not have adequate data to guide our treatment selection. Therefore, clinical experience and extrapolation from adult data will have to serve as stand-ins. For these

patients, migraine preventive treatments that have been shown to be effective in adults and can be considered to treat children and adolescents include: propranolol, amitriptyline, topiramate, candesartan, venlafaxine, memantine, and sodium valproate. In treating adolescent girls of reproductive age, it is important to note that topiramate, sodium valproate, and angiotensin receptor antagonists (eg, candesartan) have known teratogenicity.[69–71]

Acute Migraine Treatment in Children and Adolescents

This section focuses on treating pediatric acute migraine in the outpatient setting,[72] as this is where the majority of attacks are treated.

CONSIDER THE ENVIRONMENT. Children will often naturally seek out dark, quiet spaces when they have migraine. This should be encouraged. They should also be encouraged to take frequent small sips of water to remain hydrated. If they are in a place where they can get to sleep, sleep may be useful in terminating a migraine attack.

As acute medications are most effective when taken while pain is still mild,[73] which tends to be early in an attack, families and adolescents should work out strategies to ensure the medications are available and on hand. At school, adolescents who are old enough to administer their own medications might keep them in a purse or a locker. Younger children will need to go to the nurse's office or get help from an adult to administer medication. Arrangements for excusing them from class in such settings should be put in place ahead of time.

In the United States, 504 plans allow children and teenagers to have necessary accommodations at school for management of a medical condition, such as migraine. All children and adolescents with migraine should have an annual letter from their doctor stating their diagnosis and supporting accommodations for their 504 plan (**SDC 8-1**, *links.lww.com/CONT/A253*).

NONORAL ROUTES OF MEDICATION ADMINISTRATION. During acute migraine or exacerbations of chronic migraine, nausea/vomiting may make oral administration of medications challenging. Vomiting can sometimes be a very prominent part of the migraine attack in young children. In an urgent care or emergency department setting, IV administration is possible. However,

Main Exclusion Criteria for Childhood and Adolescent Migraine Prevention Trial[a] **TABLE 8-2**

A	Continuous headache
B	Accompanying medication overuse, defined as unwilling to avoid taking nonspecific analgesics/nonsteroidal anti-inflammatory drugs >3 times per week or triptans >6 times per month
C	Pediatric Migraine Disability Assessment score of ≥140
D	Current use of disallowed medications such as opioids, barbiturates, benzodiazepines, selective serotonin reuptake inhibitors, serotonin norepinephrine reuptake inhibitors, antipsychotics, antimanics, nutraceuticals, sedatives, muscle relaxants, tramadol
E	Psychiatric disease such as major depression, generalized anxiety disorder

[a] Data from Hershey AD, et al, Headache.[68]

ideally patients have the tools they need to treat successfully at home. Nasal spray or nasal powder formulations are available for some triptans, dihydroergotamine, and the NSAID ketorolac. Some children are accepting of nasal administration while others find the sensation unpleasant. Nasal absorption may be variable. The suppository route allows for excellent and rapid absorption. Prochlorperazine is available as a suppository and can be helpful for all aspects of migraine, including nausea/vomiting. Other medications can be compounded into a suppository form, including chlorpromazine, dihydroergotamine, and sumatriptan. Young children are often very accepting of a suppository; teenagers are less likely to be enthusiastic. Sumatriptan is available as a 6 mg auto injector, and smaller dosages can be drawn up in a syringe. Certain other medications can also be given by injection (eg, dihydroergotamine or ketorolac). Neurostimulation devices, such as transcranial magnetic stimulation devices or the transcutaneous electrical nerve stimulation device, could be useful acutely, although patients may not have access to these devices. The antiemetic granisetron is available as a transdermal patch. With a little trial and error, usually a nonoral treatment plan can be found.

PILL SWALLOWING. Younger children may not yet have the ability to swallow pills. Some acute migraine treatments are available as liquids, melts, or nasal sprays. Starting around age 8, neurodevelopmentally typical children can start working on pill-swallowing techniques. Practicing pill swallowing using small chocolate chewable candies or similar treats can be helpful and is often a good way to get the child to comply with the process.

ACETAMINOPHEN. Acetaminophen has been studied in a randomized, double-blind, placebo-controlled trial and was found to be effective for acute migraine in children 4 years and older.[74] Dosing is 15 mg/kg orally. Acetaminophen is available over the counter in the United States in a flavored liquid formulation at a concentration of 160 mg/5 mL. There are also 160 mg melts for older children, and 325 mg to 500 mg tablets are available over the counter. An IV formulation of acetaminophen is available and could be useful in the emergency department setting.

NONSTEROIDAL ANTI-INFLAMMATORY DRUGS. Ibuprofen has been studied in randomized, double-blind, placebo-controlled trials and found to be effective for acute migraine treatment in children.[74] Children as young as age 4 years were included in one of these studies.[74] Dosing is 7.5 mg/kg to 10 mg/kg,[74,75] generally to a maximum of 600 mg to 800 mg orally up to every 6 hours. Ibuprofen is broadly used to treat pain and fever in pediatric patients, including in infants 6 months of age and older. It is available over the counter in the United States in flavored liquid formulation at a concentration of 100 mg/5 mL. For slightly older children, 100 mg melts are available. Once children are able to swallow pills, they can take the 200 mg over-the-counter tablets with which most parents/guardians are familiar.

Naproxen has a longer half-life than ibuprofen and is perhaps better studied for acute migraine treatment in adults. Combining naproxen with sumatriptan increases the likelihood of being pain free at 2 hours and decreases the likelihood of recurrent headache from 2 to 24 hours in adults.[76] Naproxen

combined with sumatriptan has been studied in adolescents and was found to be safe and effective.[77] Naproxen dosing is 5 mg/kg to 10 mg/kg, generally to a maximum of 660 mg (3 of the 220 mg over-the-counter tablets) orally up to every 12 hours. For younger children, naproxen is available by prescription as a liquid at a concentration of 125 mg/5 mL.

Ketorolac is available as oral tablets, nasal spray, and by injection (IM/IV). In the emergency department setting, ketorolac was not as effective as prochlorperazine at treating acute pediatric migraine.[78] Some patients with significant nausea/vomiting may appreciate the option of the nasal spray formulation.

Diclofenac is available as a tablet. The individual child or adolescent with migraine might try several different NSAIDs before settling on the one that seems most effective.

TRIPTANS. Triptan medications were developed specifically for treatment of acute migraine. Seven are available on the market in the United States. Of these, four are FDA-labeled for acute migraine treatment in adolescents 12 to 17 years of age: almotriptan (oral), zolmitriptan (nasal spray), rizatriptan (melt), sumatriptan/naproxen (oral); and one medication, rizatriptan (melt), is labeled for use in children age 6 and older. TABLE 8-3 shows FDA-labeled dosing when available and shows the author's dosing recommendation where it is not.[79–87]

PRESCRIBING A TRIPTAN TO A CHILD OR ADOLESCENT. If a child's or adolescent's migraine attacks are not responsive to NSAIDs or are inadequately responsive, then a triptan is indicated. The majority of triptan contraindications are rare in pediatric patients as children tend to be healthy from a vascular standpoint. Those with a history of stroke or peripheral vascular disease would not be candidates. Blood pressure should be checked to ensure the child does not have uncontrolled hypertension. Children and adolescents who are on selective serotonin reuptake inhibitors (SSRIs) or serotonin norepinephrine reuptake inhibitors (SNRIs) generally do not need to have their access to triptans restricted. The action of triptans is specifically at 5-HT_{1B} and 5-HT_{1D} receptors, whereas serotonin syndrome results from overactivation predominantly at 5-HT_{2A} receptors. The potential for serotonin syndrome developing from combining SSRIs/SNRIs with triptans has been examined, and the risk appears to be quite low. Pharmacists concerned about this possibility can be referred to the 2010 position paper from the American Headache Society.[88]

Sumatriptan oral tablets will often be the first triptan tried in this age group simply because it is tier 1 on most insurance plans. For children younger than age 6 who require triptans, consider referral to a pediatric headache subspecialist.

For children and adolescents with chronic migraine who may have daily or even continuous headache, it is also reasonable to consider triptans for treating these headache exacerbations. While triptans are most likely to be effective if taken when pain is still mild,[73] which tends to be early on in an attack, they can still be effective when pain is moderate or severe,[76] and it is in these settings that youths with continuous headache would most likely use them. Children with chronic migraine are less likely to respond to triptans than those with episodic migraine, but many still do.[89] Counseling about frequency of use is

KEY POINTS

- Four triptans are labeled by the US Food and Drug Administration for acute migraine in adolescents 12 to 17 years of age: almotriptan (oral), zolmitriptan (nasal spray), rizatriptan (melt), and sumatriptan/naproxen (oral); and one medication, rizatriptan (melt), is labeled for use in children age 6 and older.
- Children and adolescents who are on selective serotonin reuptake inhibitors or serotonin norepinephrine reuptake inhibitors generally do not need to have their access to triptans restricted.

needed to ensure the patient does not develop medication-overuse headache[47]; generally, limiting triptan use to 2 days per week helps avoid this. Combining a triptan with naproxen may both improve the likelihood of efficacy and reduce the likelihood of developing medication-overuse headache.[76,90] For more information on prescribing triptans, refer to the article "Acute Treatment of Migraine" by Bert B. Vargas, MD, FAAN, FAHS,[91] in this issue of *Continuum*.

DIHYDROERGOTAMINE. This migraine-specific ergot derivative can be given to children via a nasal spray, IM injection, or IV. Nausea is the most common significant side effect and is most likely to occur with IV administration as the C_{max} (peak serum concentration) is higher.[92] Nonetheless, given how common nausea is in migraine already, premedicating with an antiemetic is

TABLE 8-3 Triptan Dosing in Children and Adolescents[a]

Medication	<40 kg (88 lb)	≥40 kg (88 lb)	Notes
Sumatriptan tablet	12.5–25 mg	50–100 mg	Combined sumatriptan/naproxen is labeled by the US Food and Drug Administration (FDA) for ages 12 to 17 years: 10 mg/60 mg to 85 mg/500 mg[77]
Sumatriptan nasal spray[79–82]	5 mg	10–20 mg	Studied in children aged 6 and older; labeled in Europe for ages 12 to 17 years
Sumatriptan nasal powder	11 mg	11–22 mg	Not specifically studied in children
Sumatriptan subcutaneous injection	0.1 mg/kg	4–6 mg	Doses <6 mg will typically need to be drawn up in a syringe
Rizatriptan (melt or tablet)[83,84]	5 mg	10 mg	Doses are FDA labeled for ages 6 to 17 years, by weight
Zolmitriptan tablet[85]	2.5 mg	5 mg	
Zolmitriptan nasal spray[86]	2.5 mg	5 mg	FDA labeled for ages 12 to 17 years
Almotriptan tablet[87]	6.25 mg	12.5 mg	FDA labeled for ages 12 to 17 years
Naratriptan tablet	1 mg	2.5 mg	Some studies of naratriptan for menstrual migraine included girls 15 years of age or older
Frovatriptan tablet	1.25 mg (1/2 tablet)	2.5 mg	Not specifically studied in children
Eletriptan tablet	20 mg	40–80 mg	Not specifically studied in children

[a] The doses listed are intended to be single doses given once in a 24-hour period. While giving a second dose of a triptan 2 hours after the first may be safe, additional efficacy has not been demonstrated.

prudent regardless of route of administration. Contraindications to dihydroergotamine in children mirror those of triptans.

DOPAMINE RECEPTOR ANTAGONISTS. Dopamine receptor antagonists can be particularly helpful for children and adolescents who have prominent nausea. Prochlorperazine 0.15 mg/kg IV (maximum 10 mg) is more effective than ketorolac 0.5 mg/kg IV (maximum 30 mg) for treating pediatric acute migraine in the emergency department setting.[78] Chlorpromazine has been studied in adults for acute migraine and can be used in children as well.[72] Coadministration of diphenhydramine with these medications can decrease the likelihood of akathisia.[93]

CASE 8-1 and CASE 8-2 demonstrate approaches to treatment of migraine in children and adolescents.

Tension-type Headache

Tension-type headache can occur in both children and adolescents.

EPIDEMIOLOGY. Prevalence estimates for tension-type headache in children and adolescents vary greatly, with some studies estimating 5% to 11%[94,95] and others estimating 29% to 58%.[96] While tension-type headache seems to be relatively common in the general pediatric and adolescent population, it is generally rare in the clinic. In an adult study, only 3% of patients coming to see their primary care doctor for recurrent headaches had tension-type headache, and 94% had migraine or probable migraine.[97] Tension-type headache affects boys and girls equally.[98]

DISABILITY. Tension-type headache in children and adolescents is generally not as disabling as migraine. Adolescents with tension-type headache have lower PedMIDAS scores than those with migraine.[98] In a study of adolescents, the vast majority of those with tension-type headache had little to no disability from it (ie, Grade 1 PedMIDAS scores).[98] Children with tension-type headache are no more likely than their headache-free peers to have below average school performance and are less likely to miss school than are children with migraine.[18] Nausea and vomiting are not present in tension-type headache, which helps to limit its disability. The presence of nausea in children with headaches has high specificity for a diagnosis of migraine.[42,43,53,71,99,100]

DIAGNOSIS. In the appendix of the *ICHD-3*, tension-type headache is classified as entirely featureless—ie, no photophobia, phonophobia, nausea, or vomiting.[1] Hence, the diagnosis is clearest when the headache disorder is entirely featureless.

EARLY CHILDHOOD SYNDROMES. The childhood episodic syndromes that may be associated with migraine do not seem to be associated with tension-type headache, suggesting that the pathophysiology and genetic underpinnings of migraine and tension-type headache in children are distinct. For example, while children with migraine are more likely to have a history of infant colic, children with tension-type headache are not.[32] Similarly, history of abdominal migraine is higher in children with migraine than in controls, but not in children with tension-type headache.[101]

TREATMENT OF PEDIATRIC TENSION-TYPE HEADACHE. No randomized, double-blind, placebo-controlled trials have been conducted to guide treatment in

KEY POINTS

- While tension-type headache exists in the general pediatric population, it is not a common reason for clinical presentation.
- Nausea is not present in tension-type headache. The presence of nausea in children with headaches has high specificity for a diagnosis of migraine.

CASE 8-1

An 8-year-old boy presented to the neurology clinic with his parents after being referred by his pediatrician for evaluation of 6 months of recurrent headaches. The headaches occurred once a week and typically occurred after school. The patient reported a "booming" pain all over his head, including the occiput. During the headaches he lay down on the couch and asked his siblings to be quiet. He experienced an upset stomach and vomited on a few occasions. He was otherwise healthy and developmentally typical. He was colicky as an infant. His parents reported that no one in the family had headaches "like his," but on further questioning his mother said she experienced headaches before her periods and that she had to lie down in a dark room and take ibuprofen.

His Pediatric Migraine Disability Assessment (PedMIDAS) score was 11, indicating mild headache-related disability. The boy's family had tried giving him acetaminophen, which was helpful sometimes, but it was not helpful for the more severe headaches or the ones with vomiting. His general and neurologic examinations were normal, and his weight was 30 kg (66 lb).

Acute Treatment Options for an 8-year-old 30 kg (66 lb) Patient	Goal Dose[a]	If Patient Can Swallow Pills	If Patient Cannot Swallow Pills
Ibuprofen 7.5–10 mg/kg	300 mg	1.5 tablets of the 200 mg over-the-counter tablet	15 mL of 100 mg/5 mL over-the-counter solution or 3 of the 100 mg over-the-counter junior strength chewable tablets
Naproxen 5–10 mg/kg	300 mg	275 mg prescription tablet or 220 mg over-the-counter tablet	12 mL of 125 mg/5mL prescription solution
Sumatriptan nasal spray	5 mg	1 spray to nare	1 spray to nare
Rizatriptan melt	5 mg	5 mg melt	5 mg melt
Sumatriptan oral	25 mg	25 mg tablet	Not applicable

[a] Goal dose refers to the oral acute treatment dose. Ibuprofen can be dosed every 6 hours as needed, and naproxen can be dosed every 12 hours as needed. While it is safe to give a second dose of a triptan 2 hours after the first if headache persists, no data suggest that this improves efficacy. Generally, this author recommends one dose of a triptan in a 24-hour period.

COMMENT

This boy has episodic migraine. No red flags were identified on the history or the examination to suggest that he needed neuroimaging. For preventive treatment, the patient should be counseled regarding the importance of regular sleep, exercise, meals, and hydration. Based on his age, 9 to 11 hours of sleep per night is recommended. His individualized water intake goal is 40 oz to 72 oz per day (see *headachereliefguide.com*[56]). His PedMIDAS score is high enough to consider offering preventive treatment. He has never been on a preventive treatment before, and based on the results of the Childhood and Adolescent Migraine Prevention (CHAMP) trial, a preventive treatment that has some expectation of benefit and a side effect profile that is similar to that of placebo should be selected. For acute treatment, a nonsteroidal anti-inflammatory drug might help him more than acetaminophen. Optimal evidence-based therapy is a nonsteroidal anti-inflammatory drug plus a triptan. Rizatriptan is labeled by the US Food and Drug Administration (FDA) in his age group. Sumatriptan tablets may be required first-line triptan therapy based on insurance requirements. If he does not yet swallow pills, now is a good time to start practicing. For episodes that are more severe, he may need a nonoral route of administration. Sumatriptan nasal spray has been studied in his age group and would be a reasonable option. Refer to the following table for acute treatment dosing examples for this 30 kg (66 lb) child. The family should be given a letter for the school supporting 504 plan accommodations for migraine. Follow-up should be in 6 to 8 weeks to reinforce lifestyle management and assess the efficacy of his first trial of preventive therapy.

pediatric and adolescent tension-type headache. Not all patients require pharmacologic prevention. Physical exercise or counseling from a nurse or physical therapist may help.[102] Riboflavin 50 mg/d may decrease the frequency of tension-type headache in children.[103] A small uncontrolled study suggests melatonin 3 mg nightly may be efficacious in pediatric tension-type headache prevention as well as in migraine.[104]

Posttraumatic Headache

According to the *ICHD-3*, posttraumatic headache must begin within 7 days of head trauma to be attributed to that injury (or within 7 days of regaining

CASE 8-2

A 16-year-old girl presented for evaluation of headaches. She used to get headaches a couple of times per month, but the frequency increased 6 months ago, and she had experienced pain "all the time" for the last 6 months. About 3 times a week the pain increased in intensity for several hours to the point that she had to go to bed. During these periods, she preferred to be in a dark, quiet room. Sometimes she became nauseated but did not vomit. The rest of the days, the headache was milder, and she was not nauseated or bothered by lights and sounds and could go about her activities. Her Pediatric Migraine Disability Assessment (PedMIDAS) score was 90, indicative of severe headache-related disability. Her pediatrician treated her with topiramate 50 mg twice daily for 2 months, but she did not find it helpful. She took ibuprofen 400 mg for the thrice weekly exacerbations, but it did not help. Her general and neurologic examinations were normal, and her weight was 60 kg (132 lb).

COMMENT

This is a teenaged girl with chronic migraine. Although some of her headache days do not meet migraine criteria, she has at least 15 days of headache per month, of which 8 or more days meet criteria for migraine, and she therefore meets *International Classification of Headache Disorders, Third Edition* criteria for chronic migraine.[1] She does not need both a migraine and a tension-type headache diagnosis. She would not have qualified for the Childhood and Adolescent Migraine Prevention (CHAMP) trial as she has continuous headache. The patient should be counseled that the combination of cognitive-behavioral therapy and medication seems to be most effective for treating chronic migraine in her age group. Lifestyle management advice is also indicated. All the preventive options discussed in the section on preventive therapy would be reasonable to consider in her case, except for topiramate, which she has already tried. For acute therapy, ibuprofen dosing could be optimized to 600 mg orally at headache onset, with repeated dosing up to every 6 hours as needed if headache persists. She also should be given a triptan and counseled to only use it up to 2 days per week. A sumatriptan 50 mg tablet taken with a naproxen 500 mg tablet would be a very reasonable starting point for her. A letter supporting the 504 plan accommodations for school and close clinic follow-up in 6 to 8 weeks round out her treatment plan.

consciousness and/or stopping medications that might impair pain perception).[1] It remains to be seen whether this 7-day cutoff is biologically meaningful in adults or in children and adolescents. The topic of concussion and its management is a burgeoning and important area of research and is beyond the scope of this article. In brief, the phenotype of posttraumatic headache in children and adolescents can be featureful (ie, migrainous) or featureless (ie, similar to tension-type headache). In the absence of randomized trials guiding posttraumatic headache treatment in this age group, treating the headache based on the underlying phenotype seems reasonable.

New Daily Persistent Headache

New daily persistent headache occurs when a headache begins out of the blue on a specific, recalled date and continues unabated for at least 3 months.[1] Some evidence suggests this disorder may occur more commonly in adolescents than in adults.[105] It is best thought of as a syndromic description, as multiple etiologies may exist that can lead to a new daily persistent headache phenotype.[106] The headache can resemble migraine or tension-type headache. Additional research is needed to determine how best to treat adolescents with new daily persistent headache. In the meantime, it seems reasonable to manage these patients based on phenotype.

Primary Stabbing Headache

Approximately 3% to 5% of children and adolescents present to headache clinic because of primary stabbing headache.[107] However, of children younger than age 6 presenting to headache clinic, as many as 12% are presenting because of primary stabbing headache.[108]

Primary stabbing headache is characterized by brief attacks of sharp pain. Duration is typically just a few seconds, although some children may experience attacks lasting several minutes.[1,108,109] The pain is typically described as a stab or series of stabs.[107,109] It can be quite severe.[109] Some children will be brought to their knees by the pain. Perhaps it is the particularly high pain intensity of primary stabbing headache when it occurs in the young developing brain that makes it a more common reason for children and adolescents to come to clinical attention, although not all children report severe pain intensity.[108]

The location of the pain can be anywhere in the head and can be unilateral or bilateral.[108,109] Location can change from attack to attack or be fixed. In adults, fixed location is seen in approximately one-third of patients[110]; however, it is less clear how often fixed headache location occurs in children, making it difficult to assess how clear of an indication for neuroimaging this is, particularly as young children require anesthesia for MRI scans. The complete absence of cranial autonomic symptoms is important in distinguishing primary stabbing headache from trigeminal autonomic cephalalgias.[1] Migratory location is also a helpful feature in distinguishing primary stabbing headache from a trigeminal autonomic cephalalgia. Boys and girls seem equally likely to be affected.[109,111] Onset can be in childhood or adolescence,[107–109,111] but younger than age 6 seems to be more common (CASE 8-3).[108,111] The underlying pathophysiology of primary stabbing headache is unknown; however, given that attack locations often vary within an individual, peripheral mechanisms seem less likely.[107,111] Intermittent

KEY POINTS

- **Primary stabbing headache is a particularly common reason for clinical presentation in children younger than the age of 6 years.**
- **Primary stabbing headache pain intensity can be severe in children.**

dysfunction in central nociceptive processing or brain immaturity leading to central hyperexcitability have been proposed.[107,108]

Usually, attacks are rare and short enough that they do not require any specific treatment. Reassurance about the benign nature of the headaches is typically all that families need. However, preventive treatment may be considered in cases where the attacks are frequent and distressing. Indomethacin is useful for some adult patients.[107,110] Some patients will respond to nightly melatonin.[112,113] In young children who are less than 20 kg (44 lb), melatonin 1 mg to 3 mg nightly may be sufficient. Gummy, melt, or liquid/edible melatonin formulations are available.

Trigeminal Autonomic Cephalalgias

Trigeminal autonomic cephalalgias are rare in children but do occur. Data in the pediatric and adolescent age range are limited to case reports. In the developing brain, the phenotype of a developing trigeminal autonomic cephalalgia may not yet cleanly divide out as cluster headache, paroxysmal hemicrania, hemicrania continua, or short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing (SUNCT)/short-lasting unilateral neuralgiform headache attacks with cranial autonomic symptoms (SUNA) (CASE 8-4).

Hypnic Headache

Hypnic headache is almost unheard of in children. Hypnic headache, or "alarm clock headache," is largely a disorder of older adults and is thought to be related to age-related decline in function in the suprachiasmatic nucleus of the hypothalamus.[1] However, it is possible that there could be developmental

CASE 8-3

A 3-year-old girl was brought to the headache clinic by her parents for evaluation of brief but extremely intense stabs of head pain that had been occurring multiple times per day for the last 3 months. When attacks occurred, she grabbed her head and started to cry. The location of the attacks was sometimes on the right, sometimes on the left, and could be frontal or temporal. No associated cranial autonomic symptoms were present.

General and neurologic examinations were normal, and her weight was 17 kg (37.5 lb). Her development had been normal, and she was otherwise healthy. The parents wanted to know what was causing the headaches and how to make them go away. A trial of melatonin 2.5 mg gummy nightly resolved her attacks within a week.

COMMENT

Primary stabbing headache is a surprisingly common reason children, particularly young children, present to pediatric headache clinic. Absence of cranial autonomic symptoms helps to differentiate it from trigeminal autonomic cephalalgias. It usually does not require treatment but may when attacks are frequent or particularly painful.

abnormalities in the structure or function of the hypothalamus that could lead to this disorder occurring in children. A case series of five children with hypnic headache has been reported. The children ranged in age from 7 to 11 years, with three boys and two girls. Two responded to treatment with melatonin.[114] Given that pediatric hypnic headache is remarkably rare, consider referral to a pediatric headache specialist.

CONCLUSION

Headache is common in children and adolescents. Most children who come to see the neurologist for headaches will have a primary headache disorder, with migraine being most common in this setting. For acute migraine treatment, acetaminophen and NSAIDs have been studied in children age 4 and older and have been found to be effective. Triptans are also effective in children and adolescents. Four triptans are now FDA-labeled for acute migraine treatment in adolescents, and rizatriptan is labeled for use in children age 6 and older. Unless there is a contraindication, children and adolescents whose migraine attacks do not respond to NSAIDs should be offered a triptan.

For preventive migraine treatment, the recent CHAMP trial indicates that approximately 60% of children and adolescents with migraine will improve with a three-pronged treatment approach that includes lifestyle management counseling; evidence-based optimally dosed acute therapy, specifically NSAIDs and triptans; and a daily preventive treatment that has some evidence for efficacy and a side effect profile that is similar to that of placebo. For the approximately 40% of children and adolescents who do not respond to a first-line preventive, and for those who have continuous headache and/or medication overuse who would not have qualified for CHAMP, the clinician's

CASE 8-4

A 17-year-old boy presented for evaluation of attacks of side-locked left retro-orbital pain that lasted 1 to 2 hours in duration, occurred 1 to 3 times per day, and were associated with conjunctival injection and lacrimation. Between attacks he was completely pain free. The attacks remitted completely on indomethacin.

COMMENT

The duration and frequency of this boy's attacks would be most suggestive of cluster headache in the adult; however, his absolute response to indomethacin is more suggestive of paroxysmal hemicrania. This is an example of how trigeminal autonomic cephalalgias may be phenotypically variable in the developing brain. The appendix section of the *International Classification of Headache Disorders, Third Edition* classifies these cases as an undifferentiated trigeminal autonomic cephalalgia: "A trigeminal autonomic cephalalgia–like disorder occurring in children and adolescents with characteristics of the disorder not fully developed."[1] More research is needed to understand these rare disorders in the developing brain. Referral to a pediatric headache specialist is recommended for diagnosis and treatment.

best judgment remains the best guide to therapy selection. Future research should focus on this population of children and adolescents who have migraine that is more difficult to treat, as arguably they are the ones most in need of effective preventive therapies.

USEFUL WEBSITE

INTERNATIONAL CLASSIFICATION OF HEADACHE DISORDERS, THIRD EDITION (ICHD-3)
The online version of the *ICHD-3* is a useful resource for accessing a complete listing of the diagnostic criteria of the unusual headache disorders discussed in this article.
ichd-3.org/wp-content/uploads/2018/01/The-International-Classification-of-Headache-Disorders-3rd-Edition-2018.pdf

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DISCLOSURE

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