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Pediatric Migraine

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Learning Objectives

After completing this article, readers should be able to:

1. Recognize the diagnostic criteria for pediatric migraine.
2. Describe the clinical spectrum of migraine in children and adolescents.
3. Discuss the acute and preventive treatments of migraine.

Introduction

Headache is a common chief complaint in pediatric offices and may be a symptom of a host of illnesses from viral infection to intracranial neoplasm to migraine. The clinical spectrum of migraine represents a significant subset of headache, occurring typically as recurrent, episodic attacks of head pain plus a variety of accompanying symptoms, separated by symptom-free intervals. Its most common form, migraine without aura, is characterized as intense frontal or temporal headache lasting from 1 to 48 hours, accompanied by autonomic symptoms such as nausea, vomiting, and sensitivity to light and sound. Occasionally, migraine with aura in children is accompanied by dramatic neurologic signs and symptoms such as hemiparesis, language or mental status disturbances, visual disorders, or oculomotor dysfunction. This review provides an update on the current understanding of the evaluation, classification, pathophysiology, diagnostic criteria, and management of the migraine spectrum in children.

Evaluation

The evaluation of a child who has recurrent headaches begins, and in most cases ends, with a thorough medical history and complete physical and neurologic examinations. Clues to the presence of secondary causes of headache such as tumors, infection, intoxication, or hydrocephalus are uncovered through this systematic process, as is the delineation of primary headache syndromes.

The first step is taking a history. Twelve key questions that can aid in distinguishing migraine from other primary headaches (ie, tension-type or cluster) or secondary causes of headache include:

1. What is the time pattern of your headache: sudden first headache, episodes of headache, everyday headache, gradually worsening, or a mixture?
2. How and when did your headache begin?
3. How often does the headache occur, and how long does it last?
4. Do you have one type of headache or more than one type?
5. How often does the headache occur and how long does it last?
6. Are there warning signs or can you tell that a headache is coming?
7. Where is the pain located and what is the quality of the pain: pounding, squeezing, stabbing, or other?
8. Are there any other symptoms that accompany your headache: nausea, vomiting, dizziness, numbness, weakness, or other?
9. What makes the headache better or worse? Do any activities, medications, or foods tend to cause or aggravate your headaches?
10. What do you do when you get a headache or do you have to stop your activities when you get a headache?
11. Do the headaches occur under any special circumstances or at any particular time?
12. Do you have other symptoms between headaches?

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This series of questions generally provides sufficient information to reach a specific diagnosis in most cases. (1)

The roles of additional diagnostic studies such as laboratory testing, electroencephalography (EEG), and neuroimaging can be reviewed at www.aan.com. (2) The practice parameter at that site states that documentation is inadequate to support any recommendation as to the appropriateness of routine laboratory studies (eg, hematology or chemistry panels) or performance of lumbar puncture. Routine EEG is not recommended as part of the headache evaluation.

The role of neuroimaging is better defined. Data support the following recommendations:

- Routine neuroimaging study is *not* indicated for children who have recurrent headaches and normal neurologic examination findings.
- Neuroimaging should be considered for children in whom there are historical features to suggest:
  —Recent onset of severe headache
  —Change in the type of headache
  —Neurologic dysfunction
- Neuroimaging should be considered for children who have abnormal findings on neurologic examination (eg, focal findings, signs of increased intracranial pressure, significant alteration of consciousness) or the coexistence of seizures.

Caution must be exercised in interpreting these recommendations. Neuroimaging may be considered for children who have recurrent headache based on clues extracted from the medical history or findings on the neurologic examination. Many who have a "managed care" orientation have focused only on the first recommendation and have not recognized the importance of history and physical findings, which clearly place the responsibility in the hands of the clinician to decide whether to perform ancillary testing, including neuroimaging, based on clinical judgment.

Classification of Pediatric Migraine

Migraine is common in children, and its prevalence increases steadily through childhood. The mean age of onset is 7 years for boys and 11 years for girls, and the boy-to-girl ratio shifts during adolescence (Table 1). (3)

The currently accepted classification system for migraine is shown in Table 2 (www.i-h-s.org). (4) The three principal categories are migraine without aura (common migraine), migraine with aura (classic migraine), and childhood periodic syndromes that commonly are precursors of migraine. Notably absent in this classification system are "Alice in Wonderland" syndrome, benign paroxysmal torticollis, and ophthalmoplegic migraine, but because these clinical entities present during childhood, they will be discussed.

Table 1. The Prevalence of Migraine Headache Through Childhood

By Age:	3 to 7 y	7 to 11 y	15 y
Prevalence:	1.2% to 3.2%	4% to 11%	8% to 23%
Sex Ratio:	Boys>girls	Boys=girls	Girls>boys

Migraine Pathophysiology

Migraine now is considered to be a primary neuronal process associated with an underlying, genetically determined, hyperexcitable cerebral cortex. (5)(6) Disturbances of neuronal calcium channels lead to a lowered threshold for a variety of external or internal factors that may trigger episodes of "cortical spreading depression" (CSD). CSD represents a slowly propagating wave (~2 to 6 mm/min) of neuronal hyperpolarization followed by depolarization, which is the key initial phase responsible for both migraine aura and migraine pain.

The aura of migraine represents transient, focal so-

Table 2. Migraine Classification*

Migraine Without Aura
Migraine With Aura
Typical aura with migraine headache
Typical aura with nonmigraine headache
Typical aura without headache
Basilar-type migraine
Familial hemiplegic migraine
Sporadic hemiplegic migraine
Childhood Periodic Syndromes That Commonly Are Precursors of Migraine
Abdominal migraine
Benign paroxysmal vertigo of childhood
Cyclical vomiting
Retinal Migraine
Complications of Migraine
Chronic migraine
Status migraine
Persistent aura without infarction
Migrainous infarction
Probable Migraine

*Adapted from Oleson (4).

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matosensory phenomena such as the classic visual scotomata or distortions, but also focal features such as hemiparesis, vertigo, or aphasia. The aura now is believed to be caused by the regional neuronal depolarization and an accompanying regional hypoperfusion that is observed with CSD.

The pain of migraine also is triggered by CSD through activation of the trigeminovascular system. CSD initiates vascular dilation, with extravasation of plasma proteins from dural vessels. This process produces a sterile, "neurogenic" inflammation around dural and pial vessels, mediated principally by neuropeptides and calcitonin gene-related protein. This inflammatory cascade stimulates nociceptive afferents (pain circuits), leading to activation and "sensitization" of trigeminal vascular pain afferents. Furthermore, both peripheral and central afferent circuits become so hypersensitive that virtually any stimulation–mechanical, thermal, or chemical–is perceived as painful: the concept of "allodynia." (7)(8)(9)

Migraine Without Aura

This is the most frequent form of migraine (60% to 85%). The diagnostic criteria are shown in Table 3.

Migraine With Aura

The group of disorders within the migraine with aura spectrum reflects the concept that the focal features such as visual disruptions, hemiparesis, and aphasia are clinical manifestations of the regional neuronal depolarization and hypoperfusion caused by CSD during the aura phase. The diagnostic criteria are shown in Table 3.

Approximately 15% to 30% of pediatric patients who have migraine report visual disturbances, distortions, or obscuration before or as the headache begins that start gradually and last for several minutes (typical aura). The most frequent forms are binocular visual impairment with scotoma (77%), distortion or hallucinations (16%), and monocular visual impairment or scotoma (7%). (10) Formed illusions (eg, spots, balloons, colors, rainbows) or other bizarre visual distortions (eg, "Alice in Wonderland" syndrome) may be described.

Sudden images and complicated visual perceptions should prompt consideration of benign occipital epilepsy. Transient visual obscurations also may occur in patients who have idiopathic intracranial hypertension.

Two forms of migraine with aura, both rare in children, are "typical aura with nonmigraine headache" and "typical aura without headache." In the former, the visual or sensory aura precedes a tension-type, cluster, or other primary headache syndrome. Affected patients likely are experiencing overlap syndromes, with the presence of two or more primary headaches (ie, cluster-migraine). The latter entity represents the phenomenon of a classic visual aura, but no headache occurs.

Table 3. Diagnostic Criteria for Pediatric Migraine*

Migraine Without Aura

A. At least five attacks fulfilling criteria B–D (below)
B. Headache attacks lasting 1 to 72 h
C. Headache having at least two of the following characteristics:
   1. Unilateral location, may be bilateral, frontotemporal (not occipital)
   2. Pulsing quality
   3. Moderate or severe pain intensity
   4. Aggravation by or causing avoidance of routine physical activity (eg, walking, climbing stairs)
D. During the headache, at least one of the following:
   1. Nausea or vomiting
   2. Photophobia and phonophobia, which may be inferred from behavior
E. Not attributed to another disorder

Migraine With Aura

A. At least two attacks fulfilling the criteria B–D (below)
B. Aura consisting of at least one of the following, but no motor weakness:
   1. Fully reversible visual symptoms, including positive features or negative features (eg, flickering lights, spots, or lines)
   2. Fully reversible sensory symptoms, including positive features (ie, pins and needles) or negative features (ie, numbness)
   3. Fully reversible dysphasic speech disturbances
C. At least two of the following:
   1. Homonymous visual symptoms or unilateral sensory symptoms
   2. At least one aura symptom develops gradually over ≥5 min or different aura symptoms occur in succession over ≥5 min
   3. Each symptom lasts ≥5 min and ≥60 min
D. Not attributable to another disorder

*Adapted from Oleson. (4)

Basilar-type Migraine (BM)

BM represents 3% to 19% of childhood migraines; its mean age of onset is 7 years. Attacks are characterized by episodes of dizziness, vertigo, visual disturbances, ataxia, or diplopia, followed by the headache. Unlike with most migraines, the pain may be occipital. The diagnostic

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Table 4. Diagnostic Criteria for Basilar-type Migraine*

A. Fulfills criteria for migraine with aura
B. Accompanied by two or more of the following types of symptoms:
   1. Dysarthria
   2. Vertigo
   3. Tinnitus
   4. Hypacusia
   5. Diplopia
   6. Visual phenomena in both the temporal and nasal fields of both eyes
   7. Ataxia
   8. Decreased level of consciousness
   9. Decreased hearing
   10. Double vision
   11. Simultaneous bilateral paresthesias
C. At least one of the following:
   1. At least one aura symptom develops gradually over ≥5 min or different aura symptoms occur in succession over ≥5 min
   2. Each aura symptom lasts >5 and ≤60 min
D. Headache fulfills criteria for migraine without aura and begins during the aura or follows aura within 60 min

*Adapted from Oleson. (4)

Table 5. Diagnostic Criteria for Familial Hemiplegic Migraine*

A. Fulfills criteria for migraine with aura
B. Aura consists of fully reversible motor weakness and at least one of the following:
   1. Fully reversible visual symptoms, including positive features (eg, flickering lights, spots, or lines) and negative features (eg, loss of vision)
   2. Fully reversible sensory symptoms, including positive features (eg, pins and needles)
   3. Fully reversible dysphasic speech disturbance
C. At least two of the following:
   1. At least one aura symptom develops gradually over >5 min
   2. Aura symptom lasts >5 min and <24 h
   3. Headache that fulfills criteria for migraine without aura begins during the aura or follows the onset of aura within 60 min
D. At least one first-degree or second-degree relative has had an attack
E. At least one of the following:
   1. History and physical and neurologic examination findings not suggestive of any organic disorder
   2. History or physical or neurologic examination findings suggest such a disorder, but it is ruled out by appropriate investigations

*Adapted from Oleson. (4)

criteria require two or more symptoms and emphasize bulbar and bilateral sensorimotor features (Table 4).

Familial Hemiplegic Migraine (FHM)

FHM is an uncommon autosomal dominant form of migraine, with the aura caused by a mutation in calcium channel gene *CACNA1A* linked to chromosome 19p13. Clinically, FHM is a migraine headache heralded by an aura that has "strokelike" qualities, producing some degree of hemiparesis (Table 5). Such transient episodes of focal neurologic deficits precede the headache by 30 to 60 minutes, but occasionally extend well beyond the headache itself (hours to days). The location of headache often, but not invariably, is contralateral to the focal deficits.

The diagnosis of FHM can encompass patients who present with the abrupt onset of focal neurologic signs or repetitive episodes of focal neurologic symptoms without family history.

Periodic Syndromes of Childhood That Represent Precursors of Migraine

Three childhood conditions are included in this category: benign paroxysmal vertigo, cyclic (or cyclical) vomiting syndrome (CVS), and abdominal migraine. A fourth, benign paroxysmal torticollis, is discussed in this section because recent molecular genetic information has demonstrated linkage to migraine.

Benign paroxysmal vertigo occurs in young children and is characterized by abrupt episodes of unsteadiness or ataxia. The child may appear startled or frightened by the sudden loss of balance. Witnesses may report nystagmus or pallor. Verbal children may describe dizziness and nausea. The spells may occur in clusters that typically resolve with sleep. In series that include long-term follow-up, many affected patients eventually develop BM. The diagnosis of benign paroxysmal vertigo is based on a characteristic clinical history, but caution must be exercised to exclude seizure disorders (eg, benign occipital epilepsy), otologic pathology, posterior fossa or cervical spine abnormalities, and metabolic disorders.

A pattern of cycling episodes of vomiting may be associated with a variety of gastrointestinal, neurologic, and metabolic disorders, but a significant subset of children who have stereotypical episodes of vomiting have a migrainous basis for their symptoms that represents CVS. The key clinical feature of CVS is recurrent epi-

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Table 6. Diagnostic Criteria for Cyclic Vomiting Syndrome*

Description
Recurrent episodic attacks, usually stereotypical in the individual patient, of vomiting and intense nausea. Attacks are associated with pallor and lethargy. Symptoms resolve completely between attacks.

Diagnostic Criteria
A. At least 5 attacks fulfilling criteria B and C
B. Episodic attacks, stereotypical in the individual patient, of intense nausea and vomiting lasting 1 to 5 d
C. Vomiting during attacks occurs at least 5 times/h for at least 1 h
D. Patient is symptom-free between attacks
E. Not attributed to another disorder. History and physical examination findings do not include signs of gastrointestinal disease.

*Adapted from Oleson. (4)

Table 7. Diagnostic Criteria for Abdominal Migraine*

Description
An idiopathic recurrent disorder occurring primarily in children and characterized by episodic midline abdominal pain manifesting in attacks lasting 1 to 72 h, with normality between episodes. The pain is of moderate-to-severe intensity and associated with vasomotor symptoms, nausea, and vomiting.

Diagnostic Criteria
A. At least 5 attacks fulfilling criteria B-D
B. Attacks of abdominal pain lasting 1 to 72 h
C. Abdominal pain has all of the following characteristics:
1. Midline location, periumbilical or poorly localized
2. Dull or "just sore" quality
3. Moderate or severe intensity
D. During abdominal pain, at least 2 of the following:
1. Anorexia
2. Nausea
3. Vomiting
4. Pallor
E. Not attributed to another disorder. History and physical examination findings do not suggest gastrointestinal or renal disease, or such disease has been ruled out by appropriate investigations

*Adapted from Oleson. (4)

sodes of severe vomiting with intervening wellness (Table 6).

The episodes occur on a regular, often predictable basis every 2 to 4 weeks, last 1 to 2 days, and commence in the early morning hours. The age of onset is about 5 years, and boys are affected as often as girls. The age of diagnosis is about 8 years, with the most children "outgrowing" their symptoms by age 10 years. However, a significant proportion of patients have symptoms through adolescence and even as young adults.

After a diagnostic investigation has excluded other causes of the cyclic vomiting pattern, comprehensive treatment, including both acute and prophylactic measures, may be instituted. The mainstay of acute treatment is aggressive hydration, sedation, and an antiemetic agent. Oral or intravenous (IV) hydration with a glucose-containing solution is essential. Antiemetic choices include ondansetron (0.3 to 0.4 mg/kg IV or 4 to 8 mg oral disintegrating or tablet), promethazine (0.25 to 0.5 mg/kg per dose), metoclopramide (1 to 2 mg/kg up to 10 mg twice a day), or prochlorperazine (2.5 to 5 mg twice a day). Sedation with a benzodiazepine (lorazepam 0.05 to 0.1 mg/kg up to 5 mg) or diphenhydramine (0.25 to 1 mg/kg) often is necessary to ease anxiety and permit sleep. Enthusiasm for nasal (5 mg) or subcutaneous sumatriptan (~0.07 mg/kg) preparations is growing as field experience accumulates, although none of the triptans has been subjected to clinical trials for CVS and none is approved by the United States Food and Drug Administration (FDA) for cyclic vomiting.

Initiation of a migraine prophylactic agent for CVS should be strongly considered because CVS is an extraordinarily disabling condition for both the child and family. Options include the antihistamine cyproheptadine (2 to 4 mg/d), a tricyclic antidepressant such as amitriptyline (5 to 25 mg/d), anticonvulsants such as valproate (~10 to 14 mg/kg per day) or topiramate (1 to 10 mg/kg per day), a beta blocker such as propranolol, or a calcium channel blocker such as verapamil.

Abdominal migraine is characterized by episodic, vague, midline or periumbilical abdominal pain (Table 7). Abdominal migraine includes a subset of patients who have chronic, recurrent abdominal pain and features that overlap with those of migraine without aura. Abdominal migraine generally occurs in school-age children, who report recurrent attacks of dull midline or upper abdominal pain that generally lasts for hours.

As with CVS, the key to diagnosing this entity is recognizing the recurrent pattern of symptoms and excluding other gastrointestinal or renal diseases by appro-

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priate investigations. An up-to-date reference list for CVS and abdominal migraine is available at www.cvsaonline.org.

Benign paroxysmal torticollis is a rare paroxysmal movement disorder or dyskinesia characterized by attacks of head tilt alone or accompanied by vomiting and ataxia that may last hours to days. Other torsional or dystonic features, including truncal or pelvic posturing, may be seen. Attacks manifest first during infancy, between 2 and 8 months of age.

Paroxysmal torticollis is likely an early-onset variant of BM, but the differential diagnosis must include gastroesophageal reflux (Sandifer syndrome), idiopathic torsional dystonia, and complex partial seizure. Particular attention must be paid to the posterior fossa and craniocervical junction, where congenital or acquired lesions may produce torticollis. Once the diagnosis is established and the benign nature confirmed, no treatment may be required beyond reassurance.

Other Migraine Variants

"Alice in Wonderland" syndrome is included within the spectrum of migraine with aura, but the visual aura is atypical and may involve bizarre visual illusions and spatial distortions preceding an otherwise nondescript headache. Affected patients describe bizarre or distorted visual perceptions, such as objects appearing small (micropsia), large (macropsia), or far away (teleopsia) or faces appearing distorted (metamorphopsia).

Confusional migraine is another migraine variant that has perceptual distortions as a cardinal feature. Affected patients, usually boys, abruptly become agitated, restless, disoriented, and occasionally combative. The confusion phase may last minutes to hours. Once consciousness returns to baseline, the patients describe an inability to communicate, frustration, confusion, and loss of orientation to time and may not recall any headache phase. Clearly, any sudden unexplained alteration of consciousness following head injury warrants investigation for intracranial hemorrhage, drug intoxication, metabolic derangements, and epilepsy.

Clinically, confusional migraine most likely represents an overlap between hemiplegic migraine and BM. Patients who present with unilateral weakness or language disorders should be classified as having hemiplegic migraine; those who have vertiginous or ataxic patterns should be classified as having BM.

Ophthalmoplegic migraine has been removed from the migraine spectrum and placed in the group of "cranial neuralgias" because imaging evidence reveals a demyelinating-remyelinating mechanism. The key feature is painful ophthalmoparesis, but the pain may be a nondescript discomfort. Ptosis, limited adduction, and vertical displacement (as with involvement of cranial nerve III) are the most common objective findings. The oculomotor symptoms and signs may appear well into the headache phase rather than heralding the headache. The signs may persist for days or even weeks after the headache has resolved.

The migraine variants are unique to pediatrics and are a challenging group of disorders characterized by the abrupt onset of focal neurologic signs and symptoms (hemiparesis, altered consciousness nystagmus, ophthalmoparesis) followed by headache. Frequently, these ominous neurologic signs point the clinician initially in the direction of epileptic, cerebrovascular, traumatic, or metabolic disorders, and only after neurodiagnostic testing

Table 8. Biobehavioral Therapies for Pediatric Migraine

Identification of Migraine Triggers
Biofeedback
Electromyographic biofeedback
Electroencephalography
Thermal hand warming
Galvanic skin resistance feedback
Relaxation Therapy
Progressive muscle relaxation
Autogenic training
Meditation
Passive relaxation
Self-hypnosis
Cognitive Therapy/Stress Management
Cognitive control
Guided imagery
Dietary Measures
"Avoidance diets"
Caffeine moderation
Herbs
Feverfew (*Tanacetum parthenium*)
Ginkgo
Valerian root
Minerals
Magnesium
Vitamins
Riboflavin (B2)
Acupuncture
Aromatherapy

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Table 9. Pharmacologic Options for Acute Treatment of Pediatric Migraine

Drug	Dose	Available Form
Acetaminophen*	10 to 15 mg/kg per dose	Tabs 80, 160, 325 mg Syrup 160 mg/tsp
Ibuprofen*	10 mg/kg per dose	Tabs 100 chewable, 200, 400, 600, 800 mg Syrup 100 mg/tsp
Naproxen sodium	2.5 to 5 mg/kg	Tab 220 (OTC), 250, 375, 500 mg
Ergot Alkaloids		
Ergotamine tartrate†		Tabs: 1 to 2 mg at onset of attack Sublingual tabs: 2 mg
5-HT Agonists:		
Sumatriptan*†		Tabs 25, 50, 100 mg Subcutaneous injection 6 mg Nasal spray 5, 20 mg
Zolmitriptan†		2.5, 5 mg Disintegrating tabs 2.5, 5 mg Nasal spray 5 mg
Rizatriptan†		Tabs 5, 10 mg Disintegrating tabs 5, 10 mg

*Supportive efficacy and safety data in adolescents.
†Not approved for pediatric use.

does the diagnosis of migraine become apparent. Some of these entities occur in infants and young children in whom history is limited. Only after taking the history, performing the physical examination, and obtaining appropriate neurodiagnostic studies can these diagnoses be entertained comfortably. All represent diagnoses of exclusion.

Management

Once the diagnosis of migraine is established and appropriate reassurances provided, balanced and individually tailored treatment can be instituted. The first step is to appreciate the degree of disability imposed by the patient's headache. Understanding the impact of the headache on the quality of life can guide decisions regarding the appropriate therapeutic course. (11)(12)

The fundamental goals of long-term migraine treatment include: (13)

- Reduction of headache frequency, severity, duration, and disability
- Reduction of reliance on poorly tolerated, ineffective, or unwanted acute pharmacotherapies
- Improvement in the quality of life
- Avoidance of acute headache medication escalation
- Education and enabling of patients to manage their disease and enhance personal control of their migraine
- Reduction of headache-related distress and psychological symptoms

To achieve these goals, the treatment regimen must balance biobehavioral strategies and pharmacologic measures. Stress, tension, and emotional upheavals are common precipitating and exacerbating phenomena in adolescents and must be addressed as part of comprehensive treatment. Biobehavioral treatments include biofeedback, stress management, sleep hygiene, exercise, and dietary modifications (Table 8).

The basic recommendations given to migraine sufferers include getting regular sleep and exercise, moderating caffeine intake, and maintaining hydration. The role of diet remains controversial. (14) About 7% to 44% of patients report that a particular food or drink precipitates a migraine attack. (15)(16) For children, the principal dietary triggers are cheese, chocolate, and citrus fruits. Wholesale dietary elimination of a list of foods is not recommended. Elimination diets are excessive and set the stage for a battleground at home when parents attempt to enforce a restrictive diet on an unwilling adolescent, ultimately heightening tensions. A more reasonable approach is to review the list of foods believed to be linked to migraine and invite the patient to keep a headache diary and see if a temporal relationship exists between ingestion of one or more of those foods and the development of headache. If a link is found, prudence dictates avoidance of the offending food substance.

Overuse of over-the-counter analgesics (>5 times/wk) can contribute to frequent, even daily, headache patterns. This phenomenon is called analgesic overuse headache, and the leading offending agents are aspirin, ibuprofen, and acetaminophen. Patients who are overusing analgesics must be educated to discontinue the practice. Retrospective studies have suggested that this recommendation alone can decrease headache frequency. (17)(18)

The pharmacologic management of pediatric migraine has been subjected to thorough review, available online at www.aan.com, but controlled data to support evidence-based guidelines are limited. (19)(20)(21)(22) In addition, because no migraine-specific therapies are

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Table 10. Pharmacologic Options for Preventive Treatment of Pediatric Migraine

Drug	Dose	Available Form	Toxicity
Antihistamines			
Cyproheptadine	0.25 to 1.5 mg/kg	Syrup 2 mg/tsp Tab 4 mg	Sedation Weight gain
Anticonvulsants			
Topiramate	1 to 10 mg/kg per day	Sprinkles 15, 25 mg Tabs 25, 100 mg	Sedation Paresthesias Weight loss Glaucoma Kidney stones
Valproic acid	20 to 40 mg/kg per day (usual, 250 mg bid)	Syrup 250 mg/tsp Sprinkles 125 mg Tabs 250, 500 mg	Weight gain Bruising Hair loss Hepatotoxicity Ovarian cysts
Gabapentin	10 to 40 mg/kg per day	Syrup 250 mg/tsp Tabs 600, 800 mg Capsules 100, 300, 400 mg	Fatigue Ataxia Tinnitus
Antidepressants			
Amitriptyline	10 to 25 mg qhs	Tabs 10, 25, 50 mg	Sedation
Nortriptyline	10 to 75 mg qhs	Tabs 10, 25, 50, 75 mg	Weight gain
Nonsteroidal Anti-inflammatory Agents			
Naproxen sodium	250 to 500 bid	Tabs 220, 250, 375, 500 mg	Gastritis
Calcium Channel Blockers			
Verapamil	4 to 10 mg/kg per day tid	Tabs 40, 80, 120 mg SR tabs 120, 180, 240 mg	Hypotension Nausea Atrioventricular block Weight gain
Beta Blockers*			
Propranolol	2 to 4 mg/kg per day	Tabs 10, 20, 40, 60, 80 mg LA capsules 60, 80, 120, 160 mg	Hypotension Sleep disorder Decrease in stamina Depression

*AVOID in patients who have asthma, diabetes, and depression.

approved by the FDA, "expert" recommendations must be considered "off label."

Acute treatments represent the mainstay of migraine management (Table 9). The patient should be offered several acute treatment options after the initial office visit to determine what works most effectively. Regardless of the acute treatment selected, the following general guidelines must be included as part of the patient's educational process:

- Take the medicine as soon as possible after the headache begins
- Take the appropriate dose
- Have the medicine available at the location where the patient usually has the headaches (eg, school)
- Avoid analgesic overuse (>3 to 5 doses/wk of analgesic)

The agents studied most rigorously for the acute treatment of migraine are ibuprofen, acetaminophen, and sumatriptan nasal spray, all of which have shown safety and efficacy in controlled trials. Although none of the triptan agents has yet been approved by the FDA for use in children and adolescents, multiple studies have demonstrated the safety of their use in children. (23) Thus far, only sumatriptan in the nasal spray form (5 and 20 mg) has demonstrated efficacy in adolescents. (24)(25)(26) For children younger than 12 years of age, ibuprofen (7.5 to 10 mg/kg) and acetaminophen (15 mg/kg) have demonstrated efficacy and safety for the acute treatment of migraine. (27)(28)(29)

A diverse group of medications are used to prevent migraine attacks (Table 10). Their use, however, should be limited to patients whose headaches occur with suffi-

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cient frequency or severity to warrant daily treatment. Most clinical studies require a minimum of three headaches per month to justify a daily agent. A clear sense of functional disability must be established before committing to a course of daily medication. It also is useful to identify the presence of comorbid conditions (eg, depression, obesity) that suggest the relative benefit of one agent over another.

The duration of preventive treatment is controversial. In recognition of the cyclical nature of migraine, the daily agents should be used for a finite period of time. The general recommendation is to provide treatment through the calendar school year and gradually eliminate daily agents during summer vacation. Another option in younger children is to use a shorter course (eg, 6 to 8 wk), followed by slow weaning from the medicine.

For preventive or prophylactic treatment of the population of children and adolescents who have frequent, disabling migraine, flunarizine (unavailable in the United States) is the most efficacious agent, but encouraging data are emerging regarding several antiepileptic agents such as topiramate, disodium valproate, and levetiracetam as well as the antihistamine cyproheptadine and the antidepressant amitriptyline. (30)(31)(32)

Summary

Migraine represents a wide spectrum of episodic clinical entities in childhood and adolescence. Attacks of frontal or bitemporal, pounding, nauseating headache lasting 1 to 48 hours represent the most common manifestation of migraine, but a curious subset of focal neurologic disturbances also may represent migraine. The philosophy of treatment now embraces a balanced approach that includes both biobehavioral interventions and pharmacologic measures, and decisions regarding treatment are being based on the disability produced by the headaches. A growing body of controlled pediatric data regarding the acute and preventive agents for treatment of childhood migraines is emerging, thereby lessening clinicians' dependence on extrapolated adult data.

In the near future, we anticipate additional advances in understanding the neurobiology of migraine that should translate to improved care of affected pediatric patients.

References

1. Rothner AD. The evaluation of headaches in children and adolescents. *Semin Pediatr Neurol*. 1995;2:109–118
2. Lewis DW, Ashwal S, Dahl G, et al. Practice parameter: evaluation of children and adolescents with recurrent headache. *Neurology*. 2002;59:490–498
3. Stewart WF, Linet MS, Celentano DD, Van Natta M, Siegler D. Age and sex-specific incidence rates of migraine with and without visual aura. *Am J Epidemiol*. 1991;34:1111–1120
4. Oleson J. The international classification of headache disorders. *Cephalal*. 2004;24(suppl 1):1–160
5. Pietrobon D, Striessnig J. Neurobiology of migraine. *Nature Rev*. 2003;4:386–398
6. Silberstein S. Migraine. *Lancet*. 2004;31:381–391
7. Burstein R, Yarnitsky D, Goor-Aryeh I, et al. An association between migraine and cutaneous allodynia. *Ann Neurol*. 2000;47:614–624
8. Burstein R, Collins B, Jakubowski M. Defeating migraine pain with triptans: a race against the development of cutaneous allodynia. *Ann Neurol*. 2004;55:19–26
9. Burstein R, Jakubowski M. Analgesic triptan action in an animal model of intracranial pain: a race against the development of central sensitization. *Ann Neurol*. 2004;55:27–36
10. Hachinski VC, Porchawka J, Steele JC. Visual symptoms in the migraine syndrome. *Neurol*. 1973;23:570–579
11. Powers S, Patton S, Hommel K, Hershey A. Quality of life in childhood migraine: clinical aspects and comparison to other chronic illness. *Pediatrics*. 2003;112:e1–5. Available at: http://pediatrics.aappublications.org/cgi/content/full/112/1/e1
12. Powers S, Patton S, Hommell K, Hershey A. Quality of life in paediatric migraine: characterization of age-related effects using PedsQL 4.0. *Cephalal*. 2004;24:120–127
13. Silberstein SD. Practice parameter: evidence-based guidelines for migraine headache (an evidence-based review). *Neurology*. 2000;55:754–762
14. Millichap J, Yee M. The diet factor in pediatric and adolescent migraine. *Pediatric Neurol*. 2003;28:9–15
15. Stang P, Yanagihar P, Swanson J, et al. Incidence of migraine headache: a population based study in Olmsted Country, Minn. *Neurology*. 1992;42:1657–1662
16. Van den Bergh V, Amery W, Waelkens J. Trigger factors in migraine: a study conducted by the Belgian Migraine Society. *Headache*. 1987;27:191–196
17. Reimschisel T. Breaking the cycle of medication overuse headache. *Contemp Pediatr*. 2003;20:101
18. Rothner A, Guo Y. An analysis of headache types, over-the-counter (OTC) medication overuse and school absences in a pediatric/adolescent headache clinic. *Headache*. 2004;44:490
19. Lewis D, Ashwal S, Hershey A, et al. Practice parameter: pharmacological treatment of migraine headache in children and adolescents. *Neurology*. 2004;63:2215–2224
20. Victor S, Ryan S. Drugs for preventing migraine headaches in children. *Cochrane Database Syst Rev*. 2003;4:CD 002761
21. Lewis DW, Yonker M, Winner P, Sowell M. The treatment of pediatric migraine. *Pediatr Ann*. 2005;34:448–460
22. Damen L, Bruijn J, Verhagen A, et al. Symptomatic treatment of migraine in children: a systematic review of medication trials. *Pediatrics*. 2005;116;e295–302. Available at: http://pediatrics.aappublications.org/cgi/content/full/116/2/e295
23. Major P, Grubisa H, Thie N. Triptans for the treatment of acute pediatric migraine: a systematic literature review. *Pediatr Neurol*. 2003;29:425–429
24. Winner P, Rothner AD, Saper J, et al. A randomized, double-blind, placebo-controlled study of sumatriptan nasal spray in the treatment of acute migraine in adolescents. *Pediatrics*. 2000;106:989–997
25. Ahonen K, Hamalainen ML, Rantala H, Hoppu K. Nasal

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sumatriptan is effective in the treatment of migraine attacks in children. *Neurology*. 2004;62:883–887
26. Ueberall M. Sumatriptan in paediatric and adolescent migraine. *Cephalal*. 2001;21(suppl 1):210–224
27. Hamalainen ML, Hoppu K, Valkeila E, et al. Ibuprofen or acetaminophen for the acute treatment of migraine in children: a double-blind, randomized, placebo-controlled, crossover study. *Neurology*. 1997;48:102–107
28. Lewis DW, Kellstein D, Burke B, et al. Children's ibuprofen suspension for the acute treatment of pediatric migraine headache. *Headache*. 2002;42:780–786
29. Evers S, Rahmann A, Kraemer C, et al. The treatment of childhood migraine attacks with oral zolmitriptan and ibuprofen. *Neurology*. 2006;67:497–499
30. Hershey AD, Powers SW, Vockell AL, et al. Effectiveness of topiramate in the prevention of childhood headache. *Headache*. 2002;42:810–818
31. Serdaroglu G, Erhan E, Tekgul H, et al. Sodium valproate prophylaxis in childhood migraine. *Headache*. 2002;42:819–822
32. Miller GS. Efficacy and safety of levetiracetam in pediatric migraine. *Headache*. 2004;44:238–243

PIR Quiz

Quiz also available online at www.pedsinreview.org.

1. You are evaluating a 9-year-old boy for headaches that have been occurring once or twice a month for the past 6 months. He describes a headache "in the back of his head" that is preceded by approximately 10 minutes of a spinning sensation and double vision. The headaches last for about 1 day. He is normal between episodes. There is no past medical history, although his mother reports occasional migraine headaches. Findings on his examination in your office are completely normal. Of the following, the *most* likely diagnosis in this patient is:

   A. Basilar-type migraine.
   B. Benign paroxysmal vertigo.
   C. Brain neoplasm.
   D. Familial hemiplegic migraine.
   E. Ophthalmoplegic migraine.

2. A 13-year-old girl comes to your clinic because of headaches for the last 6 weeks. The headaches occur once every few days and usually are worse at night. Sometimes her left arm feels "weak" before the headache. Acetaminophen typically does not help relieve the pain. Her mother has migraine headaches, and her maternal grandfather died from complications of a brain tumor. The girl's neurologic examination results are normal, except for mildly limited lateral eye movement on the left. Her mother is concerned about a brain tumor and asks that you obtain a computed tomography (CT) scan of the head. Which of the following features would *most* likely indicate a need for a CT scan?

   A. Failure to respond to acetaminophen.
   B. Family history of brain tumor.
   C. Family history of migraines.
   D. History of weakness before the headaches.
   E. Limitation of eye movement on the left.

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3. An 11-year-old girl is brought to the emergency department by her mother because of a headache with right-side weakness for the past 12 hours. The girl noted a numbness in her right arm and leg that was followed a few minutes later by a left frontal headache. On further questioning, she also admits to seeing "floaters" before the headache. Her mother reports that the girl had a similar episode 2 months before that resolved within a few hours. She also reports that she, herself, has had headaches and weakness in the past and that these episodes usually last for a few hours. On physical examination, the girl does not exhibit dysphasia, and she reports that the headache is still present. The rest of her neurologic examination results are normal. Which of the following is the *most* likely diagnosis?

   A. "Alice in Wonderland" syndrome.
   B. Basilar-type migraine.
   C. Benign paroxymal vertigo.
   D. Confusional migraine.
   E. Familial hemiplegic migraine.

4. A 6-year-old boy presents to the clinic because of dehydration. His mother reports that he has been vomiting continuously for the past day. Additional history reveals that he has had episodes of vomiting for the past year. The episodes typically begin in the morning and last 2 days. He often requires hospitalization for dehydration during the episodes. She thinks he seems normal between the episodes. Family history is positive for migraines in both parents. On physical examination, he appears pale and has dry mucous membranes, but results of his abdominal and neurologic examinations are normal. In addition to rehydration, which is the *most* appropriate management for this patient?

   A. Administration of intravenous ondansetron.
   B. Administration of subcutaneous sumatriptan.
   C. Biofeedback therapy.
   D. Computed tomography scan of the head.
   E. Referral to nutrition for dietary restriction.

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Pediatric Migraine

Donald W. Lewis

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CORRECTIONS AND CLARIFICATIONS IN RESPONSE TO READER COMMENTS, 2007

Readers who send in their answers to the quiz questions using the paper answer sheet often add comments. Because those sheets sometimes are submitted long after the articles are published, publication of responses by authors can be delayed considerably. We present corrections and clarifications here that pertain to articles published in 2007 (volume 28).

JANUARY. In the article by Richardson on microcytic anemia (pages 5–14), question #2 presents a patient believed to have iron deficiency who does not respond to oral iron. The correct answer is given as *C. Incorrect diagnosis.* A reader questions whether answer *B. Failure to take oral iron* would be correct. Dr. Richardson replies, "Although *B* is a possibility, the Mentzer index suggests thalassemia trait (90% sensitive for beta thalassemia trait for values <13). The red blood cell distribution width may be mildly elevated in beta thalassemia and alpha thalassemia trait." (Eldibany MM. Usefulness of certain red blood cell indices in diagnosing and differentiating thalassemia trait from iron-deficiency anemia. *Am J Clin Pathol.* 1999;111:676–682)

Question #4 gives the correct answer as *B. Alpha thalassemia trait.* A reader questions why the correct answer is not *D. Beta thalassemia trait.* Dr. Richardson replies, "Alpha thalassemia trait is more common in African American people than beta thalassemia trait and a nonelevated hemoglobin A2 value rules out beta thalassemia trait as the most common type. An unusual 'delta-beta' thalassemia or 'silent carrier' beta thalassemia hypothetically could be the answer, but the best answer is alpha thalassemia trait."

FEBRUARY. In the article by Lewis on pediatric migraine (pages 43–53), 12 key diagnostic questions are listed; but questions #3 and #5 are identical. Dr. Lewis offers a new key question that can aid in distinguishing migraine from other primary headaches:

Are you having any other medical problems or are you being treated with any medications (for the headache or other purposes)?

NOVEMBER. In the article on seizures by Major and Thiele (pages 405–414), there is a discrepancy between the caption and the diagram in Figure 1, which shows scalp electrode placement in electroencephalography. The even-numbered electrodes should be placed over the right hemisphere, as indicated in the caption.

NOVEMBER. In the In Brief on hyponatremia by Farrell and Del Rio (pages 426–428), in Table 2, the third item in the left column should read, "Hypervolemic, increased intravascular volume^4."

OCTOBER, 2008. In the In Brief: Selecting Developmental Surveillance and Screening Tools (pages e52–e58), Table 2 lists screening instruments. One of the authors of the Modified Checklist for Autism in Toddlers (M-CHAT) provided a different URL for reviewing the most up-to-date information about the instrument, which is http://www2.gsu.edu/~psydlr.

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Strip of the Month: May 2009—Druzin/Arafeh

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