Headaches in Children and Adolescents

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Headaches, while often alarming to parents, are very common during childhood and become increasing more frequent during the teenage years, particularly in adolescent females. The prevalence of *headache,* in general, ranges from 37 to 51% during the elementary school years and gradually rises to 57 to 82% by the high school ages. Recurring or episodic patterns of headache or frequent headache attacks occur in about 2.5% of 7-year-olds and as many as 15% of 15-year-olds.[1] Before puberty, reports indicate that boys are affected more frequently than girls, but following the onset of puberty, headaches are reported to occur more frequently in girls.[2-5]

Headaches can be classified as due to *primary* entities such as migraine or tension-type, or the pain may result from *secondary* causes such as brain tumors, increased intracranial pressure, drug intoxications, paranasal sinus disease, or common, acute febrile illnesses such as strep or influenza.

The purpose of this review was to provide the practitioner with an overview of the spectrum of primary headaches and a practical and rational approach to the evaluation and management of children with these recurring headache syndromes. In addition, specific syndromes in the secondary headache spectrum that commonly occur in childhood will be discussed.

Robert is a 7-year-old new patient to your practice whose mother has scheduled an appointment for evaluation of his headache.

What is the appropriate workup for a child with headache?

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Clinical Evaluation

The evaluation of the child with a headache begins, and in *most* cases will end, with a thorough medical history and complete physical, including neurological, examination. Clues to the presence of *secondary* causes of headache, such as tumors, infection, intoxication, or hydrocephalus, are uncovered through this very systematic process of history and physical. *The principle indication for the performance of ancillary diagnostic testing rests on information or concerns revealed during this fundamental process.*

The Headache History

The headache database developed by Dr. A. David Rothner identifies a series of straightforward, simple questions for the patient or parent that will gather sufficient information to generate an appropriate differential diagnosis, and in most instances, to reach a specific diagnosis (Table 1).[6]

Temporal Pattern

What is the time pattern of your headache:

- sudden, first headache
- episodes of headache
- gradually worsening
- an every day headache
- a mixture of these patterns?

This key question helps determine the *temporal pattern* of the patient's headache symptom complex, as described in Table 2. Typically, children and adolescents with headache will present with one of the following patterns:

- a headache of acute onset
- recurring patterns of headache with symptom-free intervals

Table 1. Key questions to ask in the evaluation of children with headaches

Headache Data Base

1. How and when did your headache(s) begin?
2. What is the time pattern of your headache: sudden first headache, episodes of headache, and every day headache, gradually worsening, or a mixture?
3. How often does the headache occur and how long does the headache last?
4. Do you have one type of headache or more than one type?
5. Are there warning signs or can you tell that a headache is coming?
6. Where is the pain located and what is the quality of the pain: pounding, squeezing, stabbing, or other?
7. Are there any other symptoms that accompany your headache: nausea, vomiting, dizziness, numbness, weakness, or other?
8. What makes the headache better or worse? Do any activities, medications, or foods tend to cause or aggravate your headaches?
9. What do you do when you get a headache; do you have to stop your activities when you get a headache?
10. Do the headaches occur under any special circumstances or at any particular time?
11. Do you have other symptoms between headaches?
12. Are you taking or are you being treated with any medications (for the headache or other purposes)?
13. Do you have any other medical problems?
14. Does anyone in your family suffer from headaches?
15. What do you think might be causing your headaches?

Table 2. The five temporal patterns of childhood headache

1. **Acute** headache represents a single episode of head pain without prior history of similar events. In adults, the "first and worst" headache raises concerns for aneurismal; subarachnoid hemorrhage. In children, this clinical pattern is most commonly due to febrile illness related to an upper respiratory tract infection–secondary headache.
2. **Acute-recurrent** headaches imply a pattern of attacks of head pain separated by symptom-free intervals. Primary headache syndromes such as migraine or tension-type headache usually cause this pattern. Infrequently recurrent headaches are attributed to epileptic syndromes (eg, benign occipital epilepsy), substance abuse, or recurrent trauma.
3. **Chronic progressive** headache represents the most *ominous* of the temporal patterns and implies a gradually increasing frequency and severity of headache. The pathological correlate is increasing intracranial pressure. Causes of this pattern include pseudotumor cerebri, brain tumor, hydrocephalus, chronic meningitis, brain abscess, or subdural collections.
4. **Chronic nonprogressive or chronic daily headache** (CDH) represents a pattern of frequent or constant headache. CDH is generally defined as $\geq$4 months history of $>$15 headaches/month with headaches lasting $\geq$4 hours. Affected patients have normal neurological examinations. There are usually interwoven psychological factors and great anxiety about underlying organic causes.
5. **Mixed** headache pattern represents the superimposition of acute-recurrent headache (usually migraine) upon a chronic daily background pattern, and therefore, represents a variant of CDH.

- gradually progressive patterns of increasing headache
- daily or near-daily headaches

Recognition of this *one point alone* will alert the practitioner as to which patients warrant further diagnostic testing, as each of these patterns suggests its own specific differential diagnosis, which in turn, guides the need and urgency for ancillary studies.

For example, an explosive, hyperacute headache in an older adolescent, that begins suddenly while straining, suggests a vascular event such as the rupture of an aneurysm or an arterial dissection producing subarachnoid hemorrhage. In this case, emergent noncontrast computed tomographic (CT) scan followed by spinal fluid analysis is warranted. Alternatively, a child who presents with a gradually worsening headache syndrome or a headache that causes the child to awaken from sleep and vomit will likely warrant a magnetic resonance imaging (MRI) of the brain so as to visualize the posterior fossa structures. Episodic headaches with symptom-free intervals suggest a primary headache syndrome such as the migraine or tension-type headache in which the value or yield of neuro-imaging is quite low.

Frequency and Duration

How Often Does the Headache Occur and How Long Does the Headache Last? This question helps to identify the characteristic pattern of the individual headache attack. A 4-hour attack of pain that occurs once a week points toward migraine or tension-type headache. On the other hand, brief, 5- to 15-minute attacks which occur multiple times per day point toward the trigeminal autonomic cephalalgias (ie, cluster, paroxysmal hemicrania) or primary stabbing headaches.

Location and Quality

Where Is the Pain Located and What Is the Quality of the Pain: Pounding, Squeezing, Stabbing, or Other? This question must be asked carefully so as not to "lead the witness." It is thought that children will often choose the third of three alternate choices. So as to limit the influence of suggestions, first ask the child to describe, demonstrate with a gesture, or draw a picture of the pain before resorting to a list of choices. A frontal or unilateral pounding headache suggests a migraine headache, while a global squeezing quality suggests tension-type headaches. A knife-like pain in the orbital region points toward paroxysmal hemicra-

nia or cluster headaches, but also may be an early feature of optic neuritis, which subsequently is accompanied by monocular visual loss. Global pounding daily headaches are classic symptoms of idiopathic intracranial hypertension.

The presence of pain in the *occipital* region warrants special mention and a heightened sense of physician concern. Posterior fossa neoplasms, such as a medulloblastoma, may produce occipital pain since the structures within are innervated by branches of the upper cervical roots. One emergency department based study of 150 children with acute headache found only two children who identified the occipital location, but both of these had posterior fossa tumors.

Other Symptoms

Are There Any Other Symptoms That Accompany Your Headache: Nausea, Vomiting, Dizziness, Numbness, Weakness, or Other? The presence of autonomic symptoms must be carefully explored. Nausea and vomiting are cardinal features of migraine but also may be prominent features of elevated intracranial pressure with brain tumors or idiopathic intracranial hypertension (ie, pseudotumor cerebri). What is the background temporal pattern and what other associated symptoms are present? If the nausea and vomiting are occurring in the context of discrete, 4-hour attacks of pounding headache, then migraine leads the list of concerns. If the vomiting is occurring early in the morning or awakens the child whose headaches are gradually and steadily increasing in frequency and severity, then mass lesions must be sought. Vomiting with personality changes or declining school performance may be subtle symptoms of slowly increasing intracranial pressure.

Dizziness requires dissection. Does the patient mean lightheadedness, unsteadiness, or vertigo? The distinction is important because each suggests a differing pathophysiology. Lightheadedness suggests cerebral hypoperfusion or orthostasis. Many migraine sufferers will become lightheaded on standing. Unsteadiness or vertigo suggests ataxia or balance disorders pointing toward the vestibular or cerebellar systems, in which case neuro-imaging must be considered. Dizziness and vertigo heralding an intense, throbbing headache are typical features of basilar-type migraine.

Numbness or weakness likewise must be clarified. Many migraine sufferers will have a peri-oral or hand numbness (chiro-oral) as part of the "aura" or in the prelude phase of their attack. "Weakness" requires exploration as well. Many headache patients feel "weak all over," but a localizable pattern of weakness may justify neuro-imaging in search for tumors, abscess, stroke, vascular anomaly, or hemiplegic migraine.

When these associated symptoms occur through the course of the day is often important. Traditionally, morning headaches or headaches that occur primarily on awakening raise concerns about intracranial space-occupying lesions. Similarly, headaches that are triggered or precipitated by straining, accompanied by vomiting, declining school performance, personality changes, or focal neurological symptoms can indicate tumor, abscess, or hydrocephalus.

What Do You Do When You Get a Headache or Do You Have to Stop Your Activities When You Get a Headache? This question goes to the heart of disability. Do the headaches interfere with activities of daily living? A headache that stops the child in his tracks and forces him to lie down and rest, or seek comfort in a quite cool place, or to ask for medicine is more disabling than a casual mention of headache as the child passes by on the way out the door to play outside. Migraine, cluster, and paroxysmal hemicrania are disabling types of headaches, whereas tension-type may just slow the patient down a bit, but not be truly disabling.

The degree of disability imposed by the headache is an essential component of the management decision-making process. The term often used is "headache burden." Frequent disabling headaches that result in missed school days and delayed activities impose a high headache burden and deserve a more aggressive strategy for prevention. This topic will be further discussed in the treatment sections.

Do You Have Any Other Medical Problems? The database questions also help to identify the coexistence of other symptoms or signs, such as fever, recent trauma, or other medical conditions (eg, sickle cell anemia, bleeding diathesis, or autoimmune disorders). The presence of *fever* with acute headache must raise concerns for viral or bacterial meningitis, although in the majority of instances, acute headache with fever is due to self-limited illness such as a viral upper respiratory tract infection or pharyngitis. Headache accompanied by fever in the immunocompromised patient must raise concerns for opportunistic infections.

Does Anyone in Your Family Suffer from Headaches? Ask this question in an open-ended fashion using the term "headache," not a specific diagnosis such as migraine since, oftentimes, a parent may have migraine but has been mislabeled as "sinus" or "stress" headache. Migraine, one of the most common primary headache syndromes, is usually inherited and often through maternal lineage. Although family history is not one of the diagnostic criteria for migraine, it is, nonetheless, a useful clue to determining if the patient has migraine.

Further questioning should also probe the presence of any family history of other neurological disorders. Brain tumors may have an inherited pattern in conditions such as tuberous sclerosis (eg, subependymal giant cell astrocytoma), neurofibromatosis (eg, meningiomas, acoustic schwannomas, astrocytoma), or von Hippel–Lindau (eg, cerebellar hemangioblastoma). Also, certain vascular malformations may have heritable patterns (eg, cavernous angioma).

What Do You Think Might Be Causing Your Headache? This question is often the most important one to ask and addresses the inner fears of the patient and their family. The majority of families who present to the office for evaluation of their child's headache are fearful of brain tumors. The children share these same concerns; even children as young as 4 or 5 years of age harbor these fears. Teenage boys may well be the most disturbed, even though they may try hard to hide their fears. One study of children's drawings of their headaches found that over half of the teenage boys drew themselves dead or as dying, thus indicating genuine concerns about life-threatening illness underlying their headaches.

Recognizing this fact can be extremely useful in establishing patient and parental confidence and trust. At the conclusion of each headache evaluation, I try to put myself into the parent's shoes. Once I have convinced myself of the diagnosis based on history and reassured myself that the physical and neurological examinations are normal, I can confidently tell the family that there are no signs of brain tumors or anything "bad." Confident reassurance is one of the most potent therapeutic interventions. Conversely, if you have not reassured yourself as to the diagnosis, then further testing or referral may be needed. The sequence of reassurances *must* start with the clinician.

My typical dialog conveying migraine as the diagnosis starts with my facing toward both the family and the patient:

Table 3. Headache history red flags!

Historical
Age <3 years
Morning or nocturnal headache
Morning or nocturnal vomiting
Headache increased by Valsava or straining
Explosive onset
Progressively worsening over time (chronic progressive pattern)
Declining school performance or personality changes
Altered mental status
Epilepsy
Physical examination
Hypertension
Head circumference >95%
Neurocutaneous markers
Meningeal signs
Papilledema
Abnormal eye movements
Motor asymmetry
Ataxia
Gait disturbance
Abnormal deep tendon reflexes

"When families come to see me about their daughter's (son's) headaches, one of the key things they are usually worried about is brain tumors or bad things inside the head. Let me tell you now that there are no signs of brain tumors or any other bad things."

I turn toward the patient:

"You have migraine headaches and now let's talk about what that is and how we help to stop these from happening."

At this point there is often an audible sigh of relief and the first step of treatment has been taken. As stated above, confident reassurance is often our most potent treatment measures for children and adolescents with headache.

The headache history itself will, in most instances, yield the necessary information to make the correct diagnosis. Table 3 reiterates the headache red flags.

The Physical Examination

The general physical examination must include vital signs with blood pressure and temperature. Careful palpation of the head and neck for sinus tenderness, thyromegaly, or nuchal rigidity should be performed. Head circumference *must* be measured, even in the older children, because slowly progressive increases in intracranial pressure will cause macrocrania, particularly in young children. The skin must be examined for signs of a neurocutaneous syndrome, particularly neu-

rofibromatosis and tuberous sclerosis, which are highly associated with intracranial neoplasms.

Neurological Examination

Detailed neurological examination is an essential part of the evaluation. Perhaps the best way to conduct the neurological examination is to think anatomically. Each element of the examination assesses a specific region of the brain. In the headache evaluation, we are looking for any signs of increased intracranial pressure, integrity of the brain stem, asymmetry of motor or sensory systems, coordination problems, or gait disturbances:

Mental status assesses the cerebral cortex.
Cranial nerve examination checks the brain stem function and integrity.
The motor and sensory systems evaluate the descending and ascending pathways.
Coordination looks at the cerebellar and vestibular pathways.
Gait observation puts multiple systems through a dynamic challenge.

An interesting study of a large population of children with brain tumors (n = 3000) found that about two-thirds of the children had headache as one of their presenting symptoms. Of note, o*ver 98% of children with brain tumors with headache had objective neurological findings*. The key features include altered mental status, abnormal eye movements, optic disc distortion, motor or sensory asymmetry, coordination disturbances, or abnormal deep tendon reflexes.[7]

The toughest part of the neurological examination is viewing the optic nerves and looking for papilledema. Direct ophthalmoscopy can be a challenge for even the most experienced physicians, particularly in young children. The key for a successful examination of the fundus is to have the patient fix their gaze on a far point (eg, a still picture or object) and for the examiner to look at the patient's right (or left) eye with their right (or left) eye, bringing the ophthalmoscope in from the side while being careful not to obstruct the view of the target object (Fig 1). The optic disc is located nasally to the fovea, so if the patient is visually fixed on a target at the horizon level, then the examiner can "find" the disc at about a 30- to 45-degree angle to the patient. If office examination is unsuccessful, dilated ophthalmoscopic examination will be necessary.

There is a new devise available called *Panoptic* (Welsh-Allen) that has made viewing the optic nerves much easier. There is a learning curve required, but once mastered, seeing the optic nerve becomes much easier and efficient.

The value of physical and neurological examinations cannot be overstated.

Neurodiagnostic Testing

The role of further ancillary diagnostic studies such as laboratory testing, electroencephalogram (EEG), and neuro-imaging for a child or adolescent with recurring patterns of headache has been extensively reviewed in a practice parameter of the American Academy of Neurology (AAN) and is available online at www.aan.org.[8] This parameter did not address the acute headache or the headache associated with fever.

The practice parameter determined that there is inadequate documentation in the literature to support any recommendation as to the appropriateness of routine laboratory studies (eg, hematology or chemistry panels) or performance of lumbar puncture.

Routine EEG was not recommended as part of the headache evaluation. Data compiled from eight studies showed that the EEG was not necessary for differentiation of primary headache disorders (eg, migraine, tension-type), from secondary headache due to structural disease involving the head and neck, or those due to a psychogenic etiology. In addition, EEG is unlikely to define or determine an etiology of the headache or distinguish migraine from other types of headaches. Furthermore, in those children undergoing evaluation for recurrent headache who were found to have paroxysmal EEGs, the risk of future seizures is negligible.

The role of neuro-imaging is better defined. Data compiled from six pediatric studies permitted the following recommendations:

1. Obtaining a neuroimaging study on a routine basis is *not* indicated in children with recurrent headaches and a *normal* neurological examination.
2. Neuroimaging should be considered in children in whom there are *historical features* to suggest:
   Recent onset of severe headache,
   Change in the type of headache, or
   Neurological dysfunction.
3. Neuroimaging should be considered in children with an *abnormal neurological examination* (eg, focal findings, signs of increased intracranial pres-

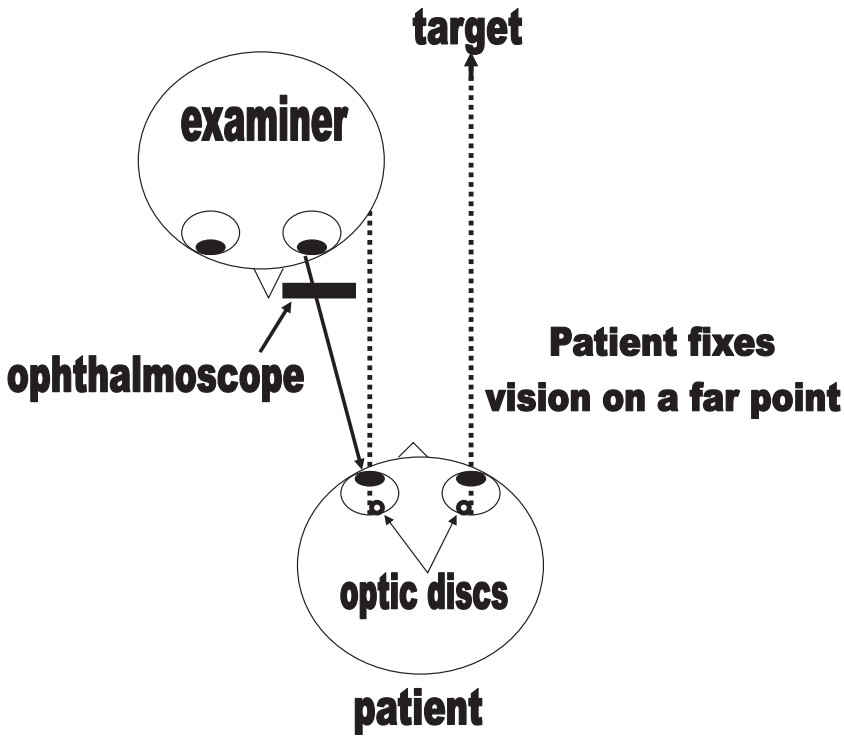

FIG 1. Seeing the elusive optic disc.

Table 4. Seeing the elusive optic disc

Ophthamoscopic examination hints:

1. The patient must have an unobstructed view to a far target.
2. The examiner must not block the patient fixation on a far target.
3. The examiner uses their left eye to view the patient's left eye (and vice versa).
4. The angle of exam is about 20 to 30 degrees to see the nasal retinal field where the optic disc will be found.
5. The examiner should first "find" the red reflex or a vessel and then ease closer to the patient to see the optic disc architecture.

sure, significant alteration of consciousness) and/or the coexistence of *seizures*.

Care must be taken not to over-, or under-, interpret these recommendations. Neuro-imaging may be considered in children with recurrent headache based on clues extracted from the medical history or based on the findings on neurological examination. Since publication of this parameter, feedback from clinicians and personal experiences have demonstrated that many in the "managed care industry" have focused only on recommendation 1 and not recognized 2 and 3, which places the responsibility clearly in the hands of the clinician to make the decision to perform ancillary testing, including neuro-imaging, based on good clinical judgment. The findings of the AAN practice parameter support the medical decision to perform scans or to withhold scans, based on clinical determinants for the individual patient.

Primary Headaches

Migraine

Migraine represents a recurring pattern of intense, disabling, pounding, or throbbing pain located around the forehead or temporal areas. As a migraine attack begins, the patient will become pale and nauseated and seek a quiet, dark room to rest. The attacks will typically last for a matter of hours but may go on for 2 to 3 days. Migraine headaches are common in children and adolescents but often go unrecognized or misattributed to causes such as sinus disease or emotional disorders.

The prevalence of migraine headache steadily increases through childhood and the male:female ratio shifts during adolescence (Table 5). The mean age of onset of migraine is 7.2 years for boys and 10.9 years for girls.[9-16]

Diagnostic Criteria for Migraine. What qualities make a headache into a *migraine* headache?

Table 5. The prevalence of migraine headache through childhood

By ages:	Preschool	Elementary school	High school
Prevalence (%):	1.2-3.2	4-11	8-23
Gender ratio:	boys > girls	boys = girls	girls > boys

Beginning in the 1950s, efforts began to define migraine in children. Valquist, and later, Prensky and Sommer, all proposed the criteria for pediatric migraine including the following:

paroxysmal headache separated by pain-free intervals,
accompanied variable number of associated features including

- visual aura
- nausea
- abdominal pain
- throbbing quality
- unilateral pain
- family history of migraine.[17,18]

In 1988, the International Headache Society (IHS) established the "gold standard" for the definition and criteria for migraine. While these criteria provided a solid framework for adult migraine, their sensitivity for the pediatric population was less than satisfactory.

In 2004, the IHS revised the diagnostic criteria and classification system in the "International Classification of Headache Disorders" (ICHD). These new criteria have incorporated many developmentally appropriate changes that will permit a broader applicability for children and adolescents while maintaining specificity and improving sensitivity.[19] The currently accepted criteria for migraine with aura are shown in Table 6.

These new criteria accept the clinical observations that pediatric migraine may be brief (~1 hour) and bifrontal in location, and the associated symptoms of photophobia and phonophobia may be *inferred* by the child's behavior, such as withdrawing to a dark, quiet room to rest during their headache attack.

Pathogenesis of Migraine. Migraine is now considered to be a primary *neuronal* process (Fig 2).[20-22] Fundamentally underlying migraine is a hyperexcitable cerebral cortex. Multiple genetic influences cause disturbances of neuronal ion channels (eg, calcium channels), which lead to a lowered threshold for a variety of external and/or internal factors that then trigger *episodes* of regional neuronal excitation followed by *cortical spreading depression* (CSD). CSD represents a slowly propagating wave (~2-6 mm/min) of neuronal depolarization and is the likely key initial phase that is responsible for (1) migraine aura, and (2) activation of the "trigeminovascular system."

Table 6. Diagnostic criteria for pediatric and adolescent migraine (I.H.S. 2004)

Diagnostic criteria:
A. At least five attacks fulfilling criteria B-D (below)
B. Headache attacks lasting 1-72 hours
C. Headache has 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 or climbing stairs)
D. During the headache, at least one of the following:
   1. Nausea and/or vomiting
   2. Photophobia and phonophobia, which may be inferred from their behavior
E. Not attributed to another disorder

The aura phase of migraine represents transient, focal somatosensory phenomena such as visual scotoma (ie, black spots, shimmering lights) or distortions, dysesthesias, hemiparesis, or aphasia. The symptoms of the aura are now thought to be caused by regional neuronal depolarization and/or the accompanying regional oligemia observed with CSD.

In addition to sustained cortical oligemia, CSD is accompanied by the extravasation of plasma proteins from dural vessels and activation of meningeal afferents. The sum of these effects is to increase c*FOS* expression in the trigeminal nucleus within the brain stem. CSD, then, is the key event for episodic activation of the trigeminal vascular system that culminates in migraine attacks.

The role played by the brain-stem nuclei is controversial. Some investigators believe the locus ceruleus and dorsal raphi nuclei act as the "migraine generator," initiating noradrenergic and/or serotonergic signals to the cortex and dural vessels in a parallel fashion. Other investigators favoring CSD as the initiating phenomena believe the brain-stem nuclei provide a "permissive" role that favors "central trigeminal hyperexcitability."

While CSD nicely explains the somatosensory aura, only about 30% of children and adolescents experience an aura. Clearly, the processes leading to *pain* may occur in the absence of a perceived aura. Two mechanisms are thought to be responsible for the generation of the pain of migraine: (1) neurogenic

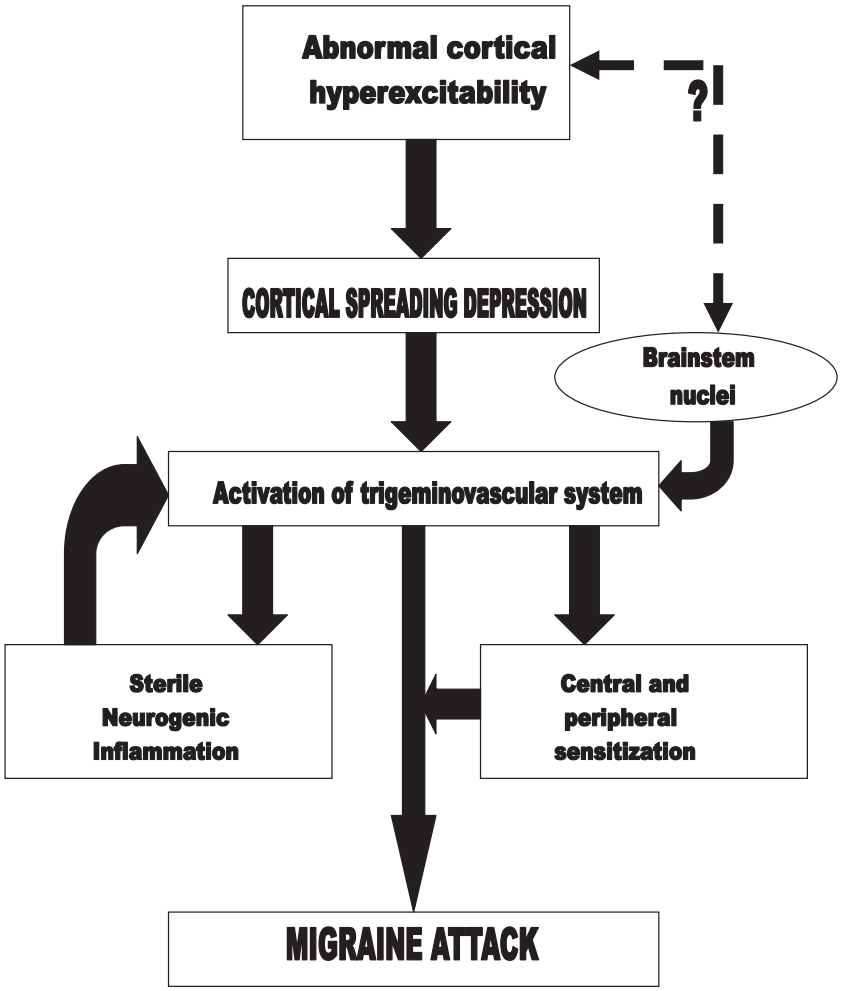

FIG 2. Migraine pathophysiology. Adapted from Peitrobon and Striessnig.[20]

inflammation of the meningeal vessels and (2) "sensitization" of peripheral and central trigeminal afferents.

As noted above, CSD initiates vascular dilation with extravasation of plasma proteins from dural vessels and activates trigeminal meningeal afferents. These processes set the stage for "neurogenic" inflammation of the dural and pial vessels, mediated principally by neuropeptides and calcitonin gene-related protein. The inflammatory cascade stimulates nociceptive afferents leading to pain. Many authors question whether neurogenic inflammation alone is sufficient to produce the pain of migraine.

One of the striking features noted during an attack of migraine is that seemingly innocuous activities, such as coughing, walking up stairs, or bending over, greatly intensify the pain. In fact, the ICHD criteria include "aggravation" by activities as one of the diagnostic features of migraine. This observation coupled with elegant research has led to the concepts of "sensitization" of trigeminal vascular afferents, whereby both peripheral and central afferent circuits become exceptionally sensitive to mechanical, thermal, and chemical stimuli. These circuits become so sensitive that virtually any stimulation is perceived as painful, the concept of "allodynia."[23-25]

Therefore, the current view of the pathophysiology of migraine begins with an inherited vulnerability to a hyperexcitable cerebral cortex. A variety of stimuli may trigger episodes of CSD, which, in turn, initiates the processes of localized, neurogenic inflammation and of sensitization of both peripheral and central afferent circuitry.

Migraine Classification. Table 7 shows the classification system for the various forms of migraine. Two clinical entities seen in children omitted from this classification are the "Alice in Wonderland" syndrome

Table 7. Migraine classification

Migraine without aura
Migraine with aura
Typical aura with migraine headache
Typical aura with non-migraine headache
Typical aura without headache
Familial hemiplegic migraine
Sporadic hemiplegic migraine
Basilar-type migraine
Childhood periodic syndromes that are commonly precursors of migraine
Cyclical vomiting
Abdominal migraine
Benign paroxysmal vertigo of childhood
Retinal migraine
Complications of migraine
Chronic migraine
Status migraine
Persistent aura without infarction
Migrainous infarction
Probable migraine

and confusional migraine; both fall within the spectrum of migraine with aura and will be mentioned in the following sections. Another syndrome in infants and young children known as paroxysmal torticollis is likely a migraine precursor and will be discussed in the section on childhood "periodic syndromes."

Migraine without aura (*common migraine*). Migraine without aura is the most frequent form of migraine seen in pediatrics, accounting for 60 to 85% of all migraine. The diagnostic criteria are shown in Table 6 and the clinical features of both migraine with and without aura are shown in Table 8.

Families or patients may recognize *prodromal* features: mood changes (euphoria to depression), irritability, lethargy, yawning, food cravings, or increased thirst. Perhaps the most frequent heralding feature is a change in behavioral patterns or withdrawal from activities.

The headache phase begins gradually and is usually frontal or temporal in location. The pain may or may not be unilateral. The quality is generally described as pounding, pulsing, and throbbing, but the key feature is its intensity. Activities will be interrupted. Photophobia and/or phonophobia are common and often prompt the adolescent to seek a quiet, dark place to rest or even to sleep, as sleep often produces significant relief.

Nausea, vomiting, and abdominal pain may be the most disabling features, as a student with headache may be able to stay in the classroom with pain, but the onset of nausea or vomiting necessitates a visit to the school nurse.

Table 8. Feature and phases of migraine without aura

Migraine without aura:
Prodromal (hours or days in advance):
Mood changes
Irritability
Euphoria
Increased thirst
Increased urination
Fluid retention
Food cravings (high CHO food)
Yawning, sighing
The headache:
Gradual onset
Escalates over minutes to hours
Lasts 2-72 hours
Frontal, bitemporal, retro-orbital, unilateral
Pounding, pulsing, throbbing
Intensity increased by activity
Autonomic symptoms:
Nausea, vomiting, anorexia
Periumbilical abdominal pain
Diarrhea
Pallor
Photophonia/photophobia
Desire to sleep
Cool extremities
Periorbital discoloration
"Goose flesh"
Increased or decreased blood pressure
Syncope
Migraine with Aura:
Visual:
Negative scotoma
"Fortification" scotoma
Field deficits, hemianopic, quadrantanopic
Photopsia
Visual distortions; teichopsia
Metamorphopsia
Prosopagnosia
Sensory:
Numbness
Tingling
Perioral numbness
Hemidysesthesias
Motor:
Hemiparesis
Monoparesis
Psychic:
Confusion
Dysphasia
Amnesia
Dysequilibrium

A migraine headache typically last hours, even days (1 to 72 hours), but does not, generally, occur more frequently than 6 to 8 times per month. More than 8 to 10 attacks per month must warrant consideration of alternative diagnoses such as organic conditions (ie, pseudotumor cerebri) or the chronic daily headache syndromes.

The time of day when the headache occurs tends to shift through childhood. Younger children will complain in the afternoon, after school. The younger teenagers will frequently report their headaches occurring about lunchtime, often precipitated by the chaos of the school cafeteria with its combination of bright lights, loud noise, and peer pressures. Older teens will acquire the more adult pattern of morning headache. This morning occurrence frequently raises the suspicion of a space-occupying lesion.

While most adolescents may readily relate these symptoms, the developmentally challenged teenager may be unable to verbalize these complaints. Caregivers will report repeated, cycling events of quiet, withdrawn behavior with pallor, regurgitation, vomiting, and desire to rest. These stereotyped episodes may prompt investigation for epilepsy, gastroesophageal reflux, or hydrocephalus, when, in fact, they may represent migraine.

Migraine with aura (*classic migraine*). Approximately 14 to 30% of adolescents will report visual disturbances, distortions, or obscuration before or as the headache begins. The aura ("cool breeze") is an *inconsistent* feature in childhood and adolescence. Often the presence of an aura must be elicited with very specific questions: "Do you have spots, colors, lights, dots in your eyes before or as you get a headache?"

Hachinski's classic report of children's visual symptoms during migraine found three dominant visual phenomena:

1. binocular visual impairment with scotoma (77%)
2. distortion or hallucinations (16%)
3. monocular visual impairment or scotoma (7%)[26]

The onset of the visual aura is gradual and lasts minutes. Sudden images and complicated visual perceptions should prompt consideration of complex partial seizures, even if followed by headache. Young adolescents may experience bizarre visual phenomena (distortions, illusions, micropsia, and macropsia) within the spectrum of the "Alice-in-Wonderland syndrome." Transient visual obscurations, brief episodes of near-complete blindness, are also features of pseudotumor cerebri.

The Migraine "Variants" and Childhood Precursors to Migraine

The migraine variants represent a heterogeneous group of disorders characterized by headache accompanied by disturbing neurological signs, such as hemiparesis, altered consciousness, nystagmus, or ophthalmoparesis. A few of these entities may manifest first in infants and young children and are considered "precursors" to more typical migraine patterns. Only after careful history, physical, and appropriate neurodiagnostic studies can these diagnoses be comfortably entertained. All of these represent diagnoses of exclusion.

Our concepts regarding the cause and mechanisms of the migraine variants have changed. The focal neurological features were once thought to occur as a result of vasoconstriction within a specific vascular distribution with resulting regional oligemia. Now, given the current views regarding the pathophysiology of migraine with aura, the focal neurological symptoms and signs that distinguish these entities represent the migraine aura with regional areas of dynamic neuronal excitation followed by depolarization and oligemia.

Table 7 depicts the ICHD categorization of the forms of migraine available online at www.i-h-s.org. Several other clinical entities, peculiar to childhood, that have links to migraine will be reviewed in this section including "Alice-in-Wonderland" syndrome (now viewed as migraine with aura), ophthalmoplegic migraine (now viewed as a cranial neuralgia), confusional migraine (often a trauma-triggered phenomenon), alternating hemiplegia of childhood (probably a metabolic disorder), and paroxysmal torticollis (a paroxysmal dyskinesia).

Basilar-type Migraine (BM). BM, also known as basilar artery or vertebro-basilar migraine, is the most frequent of migraine variants. It is estimated to represent 3 to 19% of all migraine.[27-29] The wide range of frequency relates to the rigor of the definition. Some authors included any headache with *dizziness* to be within the spectrum of BM, whereas others require the presence of objective signs or symptoms of posterior fossa involvement before establishing this diagnosis. The formal ICDH criteria require two or more symptoms and emphasize *bulbar* and *bilateral* sensorimotor features (Table 9).

The age of onset of BM tends to be in young children, with a mean age of 7 years, although the clinical entity probably appears as early as 12 to 18 months as episodic pallor, clumsiness, and vomiting in the condition know as *benign paroxysmal vertigo*.

Affected patients will have attacks of intense dizziness, vertigo, visual disturbances, ataxia, and diplopia.

Table 9. 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:
	Dysarthria
	Vertigo
	Tinnitus
	Hypacusia
	Diplopia
	Visual phenomena in both the temporal and the nasal fields of both of the eyes
	Ataxia
	Decreased level of consciousness
	Decreased hearing
	Double vision
	Simultaneous bilateral paresthesias
(C)	At least one of the following:
	At least one aura symptom develops gradually over ≥5 minutes and/or different aura symptoms occur in succession over ≥5 minutes
	Each aura symptoms lasts >5 and ≤60 minutes
(D)	Headache fulfilling criteria migraine without aura begins during the aura or follows aura within 60 minutes.

Table 10. Key clinical features of basilar-type migraine

Vertigo	73%
Nausea or vomiting	30-50%
Ataxia	43-50%
Visual field deficits	43%
Diplopia	30%
Tinnitus	13%
Vertigo	73%
Hearing loss	*
Confusion	20%
Dysarthria	*
Weakness (Hemiplegia, quadriplegia, Diplegia)	20%
Syncope	*

*No data available.

The key features of basilar migraine are shown in Table 10. These early, transient features may last for minutes or up to 1 hour and are then followed by the headache phase. Unlike the majority of migraine headaches, the pain may be occipital in location. The quality of the pain may be ill-defined and the terms such as pulsing or throbbing may not be used. A small subset of patients with BM will have their posterior fossa symptoms *after* the headache phase is well established.

The pathogenesis of BM is not well understood. While focal cortical processes, oligemia or depolarization, can explain the deficits in hemiplegic migraine, the posterior fossa signs of BM are more problematic. A single case report of a 25-year-old woman with BM exists wherein transcranial Doppler and single photon emission computed tomography (SPECT) were performed through the course of a BM attack. These data suggest decreased posterior cerebral artery perfusion through the aura phase at a time when the patient was experiencing transient bilateral blindness and ataxia.[30]

Patients experiencing posterior fossa symptoms accompanied by headache may require neurodiagnostic investigations including MRI and magnetic resonance angiography (MRA) of the brain and upper cervical cord, and EEG, in addition to metabolic studies such as an ammonia level, lactic acid, and urinary toxin and drug screens.

The management of basilar-type migraine is essentially the same as migraine with or without aura and involves analgesic medications and the prudent use of prophylactic agents, if the symptoms occur frequently enough to justify daily medications.

Familial Hemiplegic Migraine (FHM). Familial hemiplegic migraine is an uncommon, autosomal-dominant form of migraine with aura caused by a missense mutation in the calcium channel gene (CACNA1A) mapping to chromosome 19p13 in about 50% of the families. Mapping to chromosome 1q31 has been reported in other families with FHM.[3132] These discoveries of the molecular genetics of FHM have broadened our understanding of the fundamental mechanisms of migraine and demonstrated the overlap with other paroxysmal disorders such as acetazolamide-responsive episodic ataxia.[31]

Clinically, FHM is a migraine headache heralded by an aura, which has "stroke-like" qualities producing some degree of hemiparesis. The terminology is misleading since there is a wide variety of symptoms and signs beyond pure motor deficits that may accompany this migraine variant. Barlow proposed the much more appropriate term *hemi-syndrome* migraine to emphasize the diversity of associated symptoms, but unfortunately, his suggestion did not received broad acceptance.[33] The ICHD criteria (Table 11) require that some degree of hemiparesis must be present, so the term "hemiplegic" will likely persist.

The transient episodes of focal neurological deficits generally precede the headache phase by 30 to 60 minutes, but occasionally, extend well beyond the headache itself (hours to days) (Table 12). The location of the headache need not be contralateral to the focal deficits.

The appearance of acute, focal neurological deficits in the setting of headache necessitates thorough investigation for disorders such as intracranial hemorrhage, stroke, tumor, or vascular malformations. In addition,

Table 11. 2004 ICHD criteria for familial hemiplegic migraine

(A)	Fulfills criteria for migraine with aura *and*
(B)	Aura consisting of fully reversible motor weakness and at least *one* of the following:
	Fully reversible visual symptoms including positive features (eg, flickering lights, spots, or lines) and/or negative features (eg, loss of vision).
	Fully reversible sensory symptoms including positive features (eg, pins and needles).
	Fully reversible dysphasic speech disturbance.
(C)	At least *two* of the following:
	At least one aura symptom develops gradually over >5 minutes
	Each aura symptom lasts >5 minutes and <24 hours
	Headache that fulfills criteria for migraine without aura begins during the aura or follows the onset of aura within 60 minutes
(D)	At least one *first-degree or second-degree relative* has had attacks fulfilling A-C.
(E)	At least one of the following:
	History and physical and neurologic examinations not suggesting any organic disorder, history or physical or neurologic examinations suggesting such disorder, but is ruled out by appropriate investigations

Table 12. The features of hemiplegic migraine

Motor:	
	Hemiplegia, hemiparesis
	Monoplegia, monoparesis
Sensory:	
	Hemidysesthesia
	Hemihypesthesia
	Hemianesthesia
	Cheiro-oral dysesthesias
	Digito-lingual dysesthesias
Mental Status:	
	Confusion
	Dysphasia, aphasia, dysarthria
Visual:	
	Hemianopic defects
	Quandantanopic defects

complex partial seizures or drug intoxication with a sympathomimetic must be considered. Neuro-imaging (MRI and MRA) and EEG are warranted. Investigations for embolic sources or hypercoagulable states are likewise appropriate.

There are no treatment trials reported for the management of hemiplegic migraine.

Sporadic Hemiplegic Migraine. This clinical entity was recently added to the ICHD to include those patients who present with the abrupt onset of focal neurological signs or repetitive episodes of focal neurological symptoms *without* family history. The diagnostic criteria are the same as FHM except for the requirement of an affected first- or second-degree relative.

"Periodic Syndromes of Childhood" that Represent Precursors of Migraine. Four childhood conditions are included in this category: benign paroxysmal vertigo, cyclic vomiting syndrome, abdominal migraine, and benign paroxysmal torticollis. The latter is not included within the ICHD spectrum but is traditionally viewed as a precursor to migraine and evidence is mounting to its migrainous nature.

Benign Paroxysmal Vertigo (BPV) occurs in young children and is characterized by abrupt episodes of unsteadiness or ataxia. The child may appear frightened by the sudden loss of balance. Astute observers may report nystagmus or pallor. Verbal children may report dizziness and nausea. The spells may occur in clusters that typically resolve with sleep. Long-term follow-up suggest that many children with BPV evolve to migraine, specifically basilar-type migraine.

The diagnosis of BPV is one of exclusion. Epilepsy, otological pathology, and central nervous system (CNS) pathology should be ruled out before this diagnosis is tenable.

Treatment of BPV can include symptomatic treatment such as antiemetics, although sleep will stop a cluster of attacks in most patients. For a child in whom frequent events are occurring, a trial of cyproheptadine (2 to 4 mg) orally at bedtime may be effective but the duration of treatment is typically brief (4 to 6 weeks). Reassurance regarding the benign nature of the condition is generally all that is required.

Cyclic or cyclical vomiting syndrome (*CVS*) is characterized by recurrent episodes of severe vomiting with interval periods of "wellness." A distinctive feature of CVS is that, during attacks, children with CVS will experience a higher intensity of vomiting per hour (eg, >4 emesis/h) than children with other chronic vomiting from gastrointestinal causes. The episodes may occur on a regular basis and parents can often predict within a few days when the next episode is due. Children with recurring episodes of vomiting require a thorough diagnostic investigation to exclude intermittent bowel obstruction (eg, malrotation), elevated intracranial pressure (eg, hypothalamic tumors, or hydrocephalus), epilepsy (eg, benign occipital epilepsy), and metabolic disorders such as urea cycle defects and organic acidurias.

The diagnostic criteria for CVS are shown in Table 13. The age of onset is about 5 years and boys and girls are affected equally. The age of diagnosis is about 8 years and the majority of children "out grow" their symptoms by age 10; however, a significant

Table 13. 2004 ICHD criteria for cyclical vomiting

Description:
Recurrent episodic attacks, usually stereotypical in the individual patient, of vomiting and intense nausea. Attacks are associated with pallor and lethargy. There is complete resolution of symptoms between attacks.

Diagnostic criteria:

A. At least five attacks fulfilling criteria B and C
B. Episodic attacks, stereotypical in the individual patient, of intense nausea and vomiting lasting 1-5 days
C. Vomiting during attacks occurs at least five times/hour for at least 1 hour
D. Symptom-free between attacks
E. Not attributed to another disorder. History and physical examination do not show signs of gastrointestinal disease.

Table 14. 2004 ICHD criteria for abdominal migraine

Description:
An idiopathic recurrent disorder seen mainly in children and characterized by episodic midline abdominal pain manifesting in attacks lasting 1-72 hours 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 five attacks fulfilling criteria B-D
B. Attacks of abdominal pain lasting 1-72 hours
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 two of the following:
   1. Anorexia
   2. Nausea
   3. Vomiting
   4. Pallor
E. Not attributed to another disorder. History and physical examination do not show signs of gastrointestinal or renal disease or such disease has been ruled out by appropriate investigations.

proportion of patients will have symptoms through adolescence and even as young adults. The attack frequency is often 2 to 4 weeks and the duration of attacks averages about 24 to 40 hours, typically commencing in the early morning hours.

CVS is an early childhood form of migraine, which may then evolve into abdominal migraine, and, later, to typical adult-type migraine.

After a complete diagnostic workup to rule out other medical conditions, a comprehensive treatment plan may be put into place. As with migraine, acute treatments and preventive strategies may be considered. For children with infrequent episodes, one per month or less, an attempt to treat individual episodes may be considered without the initiation of prophylaxis. For acute treatment of attacks, aggressive rehydration, sedation, and an antiemetic agent represent the mainstay of therapy. 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/dose), metoclopromide (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) is often necessary. Enthusiasm for nasal (5 mg) or subcutaneous sumatriptan (~0.07 mg/kg) preparations is growing with field experiences mounting, although none of the triptans have been subjected to clinical trials for CVS and none are FDA approved.

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

An up-to-the-minute reference list for CVS and abdominal migraine is available online at *www.cvsaonline.org*.

Abdominal migraine is a new addition to the 2004 ICHD classification and is an idiopathic, recurrent disorder seen mainly in school-aged children characterized by episodic vague, midline, or periumbilical abdominal pain (Table 14). First described nearly a century ago, abdominal migraine describes a subset of children with recurrent episodes of abdominal pain that have features similar to those of migraine headache. Children with abdominal migraine report recurrent attacks of midline or poorly localized pain that is dull in nature and generally lasts for hours. As with the usual pattern of migraine headache, a particularly striking characteristic of abdominal migraine is the complete resolution of symptoms between attacks. Attacks may be associated with pallor and flushing, and parents often report dark circles under the eyes.[34] Frequently identified between the ages of 3 and 10 years of age, abdominal migraines occur in patients who have a strong family history of migraine headaches.[35]

The diagnosis of abdominal migraine requires thorough investigation for gastrointestinal causes and is excluded if any of the following is present: mild

symptoms not interfering with daily activities; burning pain; non-midline abdominal pain; symptoms consistent with food allergy or other gastrointestinal disease; attacks less than 1 hour; or the persistence of symptoms between attacks.[36,37]

Little data exist regarding the treatment of abdominal migraine; however, anecdotal evidence demonstrates that many of the guidelines used in the treatment of migraine headaches are also efficacious in the management of abdominal migraines. Russell and coworkers reported success with a series of measures that include the reassurance there is no serious abdominal pathology, as well as avoidance of triggers thought to instigate migraine headaches such as chocolate, caffeine, and amines. Patients are also encouraged to avoid both alterations in sleep patterns and skipping meals. By restricting the diet and gradually reintroducing foods, an attempt to identify specific foods that may be affecting the individual patient may be helpful. Little is reported regarding the use of drugs to manage the attacks of abdominal migraine. Medications that have demonstrated some utility include pizotifen, propranolol, and cyproheptadine.[38]

While abdominal migraine rarely persists into adulthood, longitudinal evidence suggests an evolution of abdominal migraines into the more typical migraine headaches. In one 10-year follow-up study of children who suffer from abdominal migraine, Dignan and coworkers[39] found that, while 61% reported resolution of abdominal symptoms, 70% developed classical migraine headaches.

As with CVS, the key to this entity is to recognize the recurrent pattern of symptoms and to exclude other gastrointestinal or renal diseases by appropriate investigations.

Benign Paroxysmal Torticollis (BPT) is a rare paroxysmal movement disorder characterized by episodes of head tilt or torticollis accompanied by vomiting and ataxia that may last hours to days.[40] Other dystonic (twisting) features, including truncal or pelvic posturing, were described by Chutorian.[41] The original descriptions of BPT by Snyder suggested a form of labyrinthitis and demonstrated abnormal vestibular reflexes.[42] Attacks first manifest during infancy between 2 and 8 months of age.

The link to migraine for BPT is strengthening even though the disorder was not included in the most recent ICHD classification system. Paroxysmal torticollis is likely an early onset variant of basilar migraine, which itself is a variant of benign paroxysmal vertigo. Additionally, there is often a family history of migraine. More intriguing information has recently been reported wherein four children with this clinical entity have been shown to have the mutation in the CACNA1A gene.[43]

The differential diagnosis must include gastroesophageal reflux (Sandifer syndrome), idiopathic or paroxysmal torsional dystonia, complex partial seizure; particular attention must be paid to the possibility of posterior fossa and craniocervical junction disorders (either congenital or acquired), which may produce torticollis. Rarely, fourth cranial nerve palsy (eg, troclear) may produce compensatory head tilt.

There are no clinical trials reported. Once the diagnosis of BPT is established and the benign nature is confirmed, there may be no requirement for treatment beyond reassurance. If the episodes are recurrent and disabling, management options may include a trial of cyproheptadine.

Other Migraine Variants. "*Alice in Wonderland*" syndrome represents the spectrum of migraine with aura, but the visual aura is quite atypical and may include bizarre visual illusions and spatial distortions preceding an otherwise nondescript headache. Affected patients will describe distorted visual perceptions such as micropsia, macropsia, metamorphopsia, teleopsia, and macro/microsomatognopsia. The children rarely seem frightened by these illusions and relate the experience in enthusiastic detail. Witnesses to the child's event will either remark the child has an unusual, almost bemused, look on their face or describe the child changing body positions so that they can "get under a low ceiling." Although now absorbed under the category of migraine with aura, historically, "Alice-in-Wonderland" syndrome is a distinctive migraine variant most commonly seen in children. Unusual visual-perceptual abnormalities may occur with infectious mononucleosis, complex partial seizures (particularly benign occipital epilepsy), and drug ingestions.

Confusional migraine is another migraine variant seen in children and adolescents, omitted from the 2004 ICHD, which 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. Later, once consciousness returns to baseline, the patients will describe an inability to communicate, frustration, confusion, and loss of orientation to time and may *not* recall a headache phase

at all. This disorder often follows minor head trauma and is frequently referred to as "footballers' migraine." Athletes, following vigorous scrimmage, may not remember how to get home, their phone numbers, or addresses. 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 basilar-type migraine. Patients who present with unilateral weakness or language disorders ought best to be classified as hemiplegic migraine and patients with vertiginous or ataxic patterns be classified as basilar-type migraine.

Ophthalmoplegic migraine (OM) has recently been removed from the "migraine" spectrum and moved to the group of "cranial neuralgias." Solid imaging evidence has demonstrated a demyelinating-remyelinating mechanism for OM, so this reclassification is quite appropriate. Curiously still labeled as "ophthalmoplegic *migraine*" though, this clinical entity is characterized by transient disturbances in Cranial Nerves III, IV, or VI coupled with peri- or retro-orbital pain. The key feature is *painful ophthalmoparesis* but the headache may be a minimal, nondescript retro-orbital discomfort. Ptosis, limited adduction, and vertical displacement (ie, oculomotor nerve) are the most common objective findings.

The time course of OM is quite different from that of the more commonly encountered migraine variants. Symptoms and signs of oculomotor dysfunction 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 differential diagnosis for OM includes aneurysm, mass lesion, or an inflammatory process around the orbital apex. Therefore, imaging with MRI and MRA is indicated. In those children with external ophthalmoparesis, ocular myasthenia may enter the differential diagnosis and test doses of edrophonium (Tensilon) may be indicated.

Repeated attacks of OM can lead to permanent deficits; therefore, treatment both acutely and prophylactically must be considered. Steroids are commonly given during the acute phase of the disorder. Controversy exists regarding the use of preventive therapies.

Alternating hemiplegia of childhood is a bizarre, fascinating, and rare clinical condition that was traditionally considered to be a variant of hemiplegic migraine, but now is viewed as a metabolic disease, probably within the spectrum of mitochondrial disorders or channelopathy. It has been omitted from the 2004 ICHD Classification system for migraine. Recently, however, a family with features that bridged the phenotype between familial hemiplegic migraine and alternating hemiparesis of childhood (AHC) was reported to have a novel ATP1A2 mutation suggesting a possible common pathogenesis.[44]

Affected patients have their initial symptoms before 18 months of life. These unfortunate children have attacks of paralysis: hemiparesis, monoparesis, diparesis, ophthalmoparesis, or bulbar paralysis that may be accompanied by *variable* tone changes (flaccid, spastic, or rigid). A variety of paroxysmal involuntary movements including chorea, athetosis, dystonia, nystagmus, and respiratory irregularities (hyperpnea) can be seen. The attacks of paralysis can be brief (minutes) or prolonged (days) and potentially life-threatening during periods of bulbar paralysis. Curiously, the attacks generally subside following sleep. Affected children are frequently developmentally challenged.[45,46]

The link to migraine was based on the presence of a high incidence of migraine in the families of affected children and on cerebral blood flow data that suggest a "migrainous" mechanism.

In 1997, an international workshop was conducted to address the various hypotheses surrounding AHC and the proceedings have been reviewed by Rho and Chugani.[47] Proposed mechanisms include channelopathy, mitochondrial cytopathy, and cerebrovascular dysfunction, although the former seems to be the most likely hypothesis.

The calcium channel blocker flunarezine (5 to 10 mg/d), not available in the U.S., can be remarkably effective in reducing the attack frequency and severity.

Investigations into the etiology of this entity indicate that aggressive evaluation is warranted to rule out vascular disorders, inborn errors of metabolism, mitochondrial encephalomyopathies, or epileptic variants.

The migraine variants are unique to pediatrics and are a fascinating and challenging group of disorders characterized by the onset of focal neurological signs and symptoms such as hemiparesis, altered consciousness, nystagmus, or ophthalmoparesis followed by headache. Oftentimes, these ominous neurological signs initially lead the clinician in the direction of epileptic, cerebrovascular, traumatic, or metabolic dis-

orders and only after thorough neuro-diagnostic testing does the diagnosis become apparent. Some of these entities occur in infants and young children where history is limited. Only after careful history, physical, and appropriate neurodiagnostic studies can these diagnoses be comfortably entertained. All represent diagnoses of exclusion.

Management of Pediatric Migraine

Once the diagnosis of migraine is established and your confident reassurance is provided to the patients and family, what are the best treatments for pediatric migraine?

The goals for long-term migraine management are to achieve the objectives stated in the American Academy of Neurology Practice Parameter (www.aan.org):

1. Reduction of headache frequency, severity, duration, and disability
2. Reduction of reliance on poorly tolerated, ineffective, or unwanted acute pharmacotherapies
3. Improvement in the quality of life
4. Avoidance of acute headache medication escalation
5. Education and enablement of patients to manage their disease to enhance personal control of their migraine; and
6. Reduction of headache-related distress and psychological symptoms[48]

To achieve these goals, an individually tailored treatment program must include biobehavioral strategies and nonpharmacological methods as well as pharmacological measures.

Treatment options may be divided into three basic categories:

1. Biobehavioral strategies
2. Acute therapies, and
3. Preventive measures

The first step in the tailoring process is to determine the degree of disability imposed by the patient's headaches. How often is the patient missing, coming home early from, or arriving late to, school? Are after-school or weekend activities affected? Understanding the impact of the headache on the quality of life will guide in the decisions regarding the most appropriate therapeutic course.[49,50]

The second step is to establish the pattern. How often are the headaches occurring? How long do they last? Is there a seasonal variation? How much medicine is the patient requesting per week? Headache calendars are invaluable to determine the frequency and duration of headache and to help identify precipitating or provocative phenomena. Knowledge of this pattern will guide the clinical decisions necessary to tailor the treatment to the patient.

As an example, consider an 8-year-old who has one or two intense attacks per month of frontal, pounding, nauseating headache at school starting after lunch that last for 1 to 2 hours. This qualifies as infrequent migraine attacks after lunch at school. What is happening at lunchtime? Is he the target of a bully in the cafeteria or is it the noise and chaos of the lunchroom? Could this child benefit from eating lunch in the quiet of the library or a classroom? Pharmacologically, a simple analgesic agent such as acetaminophen (15 mg/kg) or ibuprofen (7.5 to 10 mg/kg) should be readily available to the child at school and the boy must be educated to request the medicine as soon as the headache begins. This patient requires no daily preventive medications and with identification and elimination of triggers may require no medications at all.

Alternatively, consider a 16-year-old with three migraine attacks per week. Each episode lasts for more than 4 hours and she is missing about 2 days of school per month. This patient is experiencing significant disability and will likely require a blend of management options including biobehavioral interventions (eg, biofeedback), acute medicines (eg, sumatriptan or zolmitriptan nasal spray), and daily preventative agents (eg, amitriptyline, topiramate, or valproic acid) during the school year. Many patients with this pattern can be successfully taken off medicine during the summer months.

Biobehavioral Strategies. Virtually all patients with migraine will benefit from a review of the basic biobehavioral measures that include sleep hygiene, exercise, dietary modifications, biofeedback, and stress management (Table 15).[51]

Good "sleep hygiene" is essential for adolescents with frequent migraine headaches. Chaotic sleep patterns, staying up late on weekend nights, sleeping in until afternoon on Saturday and Sunday, and then getting up early for school on Monday, set the stage for Monday morning migraines. Sleep disturbances have been found to occur in 25 to 40% of children with migraine. Too little sleep (42%), bruxism (29%), cosleeping (sleeping with parents or other family member) (25%), and snoring (23%) were found among a population of 118 children using the "Chil-

Table 15. Recommended bio-behavioral program for children and adolescents with migraine

1. Good sleep hygiene
   Regular sleep schedule
   Avoid excess, inadequate, or chaotic sleep
2. Regular aerobic exercise (30 minutes/day)
3. Regular meals, avoid missing meals
4. Caffeine avoidance/moderation
5. Dietary adjustments
   "Avoidance" diets
6. Identification of migraine triggers
7. Bio-behavioral
   (a) Biofeedback
      Electromyographic biofeedback
      Electroencephalography
      Thermal hand warming
      Galvanic skin resistance feedback
   (b) Relaxation therapy
      Progressive muscle relaxation
      Autogenic training
      Meditation
         Passive relaxation
         Self-hypnosis
   (c) Cognitive therapy/stress management
      Cognitive control
      Guided imagery
   Complementary and alternative
      Herbs
         Feverfew (*Tanacetum parthenium*)
         Ginkgo
         Valerian root
      Minerals
         Magnesium
      Vitamins
         Riboflavin (B2)
   Acupuncture
      Aroma therapy

dren's Sleep Habit Questionnaire." Miller and coworkers compared children with migraine to matched controls and demonstrated statistically significant differences in sleep duration, daytime sleepiness, night awakening, sleep anxiety, parasomnias, sleep onset delay, bedtime resistance, and sleep-disordered breathing.[52] The authors of this study stated that it is unclear, however, whether sleep disturbances increased the occurrence of migraine, whether frequent and intense migraine lead to sleep disturbances, or whether the two are unrelated. Clearly, further investigation is necessary. Nonetheless, current clinical practice is to recommend good sleep hygiene.

A regular exercise program is recommended for adolescents with frequent migraines. A recent study evaluated the effects of exercise and plasma endorphin levels in 40 migraine patients. Koseoglu detected beneficial effects on all migraine parameters.[53]

The role of dietary measures has recently been reviewed by Millichap and Yee, and this topic remains controversial.[54] Seven to 44% of children and adults who have frequent migraine headaches report that a particular food or drink can precipitate a migraine attack.[55,56] In children, the principal dietary triggers where cheese, chocolates, and citrus fruits. Several other dietary precipitants including processed meats, yogurt, fried foods, monosodium glutamate, aspartamine, and alcoholic beverages also have been implicated as migraine triggers. Interestingly, for chocolate, the median time interval from ingestion to the onset of headache was 22 hours (3.5 to 27 hours).[57]

While about one-third of children with migraine may report a dietary association, *complete or wholesale dietary elimination of an arbitrary list of foods is not recommended*. Once popular, elimination diets are now judged to be excessive and generally set the stage for a battleground at home when parents attempt to enforce a restrictive diet on an unwilling adolescent, ultimately producing heightened tensions at home. A more reasonable approach is to review the list of foods traditionally linked to migraine with the patient and then invite them to maintain a headache diary to try to determine if any 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. Placing the patient in control of this experiment will aid in implementation of any dietary changes and keep the parent out of the fray.

In addition to *what* they eat, it is important to encourage regular meals and to drink plenty of fluids. Many teenagers skip breakfast routinely. Missing meals is a common precipitant of migraine and has been identified by the adolescents and children as one of the leading triggers.[58] We recommend that every patient with frequent migraine should eat three meals per day, including breakfast, and that they drink plenty of water.

Caffeine warrants special mention. A link between caffeine and migraine has been established.[59,60] Not only does caffeine itself seem to have an influence on headache, but caffeine may disrupt sleep or aggravate mood, both of which may exacerbate headache. Furthermore, caffeine-withdrawal headache, which begins 1 to 2 days following cessation of regular caffeine use, can last up to a week.[61] Every effort must be made to moderate caffeine use.

Table 16. Acute treatment for childhood migraine

Drug	Dose	Available
Acetaminophen*	10-15 mg/kg/dose	Tabs 80, 160, 325 mg Syrup 160 mg/tsp
Ibuprofen*	10 mg/kg/dose	Tabs 100 chewable, 200, 400, 600, 800 Syrup 100 mg/tsp
Naproxen sodium	2.5-5 mg/kg	Tab 220 (OTC), 250, 375, 500 mg
Combination preparations		
Butalbital, aspirin/acetaminophen, caffeine (Fiorinal, Fioricet, Esgic)	1-2 qid	
Isometheptane, acetaminophen, dichloralphenazone (Midrin)	1-2 capsules, repeat hourly, ≤5 cap/d	
5-HT agonist:		
Sumatriptan†		25 mg, 50 mg, 100 mg tabs 6 mg subcutaneous injection 5 mg, 20 mg nasal spray*
Zolmitriptan†		2.5 mg, 5 mg 2.5 mg, 5 mg oral disintegrating tablet 5 mg nasal spray
Rizatriptan†		5, 10 mg tabs 5, 10 mg oral disintegrating tablet

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

Overuse of "over-the-counter" analgesics has been a particular focus recently. Recognized in adults some years ago, overuse (>5 times/week) of acetaminophen, ibuprofen, and, to a lesser extent, aspirin-containing compounds can be a contributing factor to frequent, even daily, headache patterns. When recognized, patients who are overusing analgesics must be educated to discontinue the practice. Retrospective studies have suggested that this recommendation alone can decrease headache frequency.[62,63]

Biofeedback has demonstrated effectiveness in the treatment of both adults and children with migraine in several controlled trials. While the physiological basis for its effectiveness is unclear, data suggest that levels of plasma beta-endorphin can be altered by biofeedback therapies.[64] Biofeedback therapies commonly use electrical devices that provide audio or visual displays to demonstrate a physiological effect. Thermal biofeedback is the most commonly used technique in pediatrics. Children are taught to raise the temperature of one of their fingers. Thermal biofeedback can be easily taught to children and its use has been demonstrated to benefit both the number and the severity of migraine attacks. Once taught these methods, the children can manage future headaches, allowing them to feel greater control of their health. The logistical drawbacks are the limited availability of psychologists (or other providers) in many communities and the reluctance of "third-party" payers to cover this service.

Stress management and relaxation therapies use techniques such as progressive relaxation, self-hypnosis, and guided imagery. Controlled trials have found relaxation therapies to be as effective in reducing the frequency of migraine attacks as the beta-blocker propranolol.[65] Stress management is particularly useful in the population of high achieving and over-scheduled adolescents who can clearly link the stress of school to their headache patterns. The lessons learned with stress management may be carried forward into their college and graduate years.

Acute Treatments. Acute treatments, taken at the *onset* of the migraine attack (ie, within 20 to 30 minutes), represent the mainstay of migraine management. Although a variety of pharmacological agents are used in the acute treatment of migraine in common practice, none have an indication from the FDA for use in children. An AAN Practice Parameter, focusing on the pharmacological treatment of migraine in children and adolescents, provides a critical review of the literature regarding treatment options (Table 16).[66]

Regardless of the acute agent selected, there are several fundamental principles for acute treatment:

1. Medicine must be taken within 20 to 30 minutes of the onset of the headache,

2. The appropriate dose must be used,
3. Medicine must be available where the patient usually has their headaches (eg, school, work), and
4. Medications must not be "overused."

Analgesics. Simple analgesics and nonsteroidal antiinflammatory drugs (NSAIDs) are quite effective in children and adolescents. Ibuprofen (7.5 to 10 mg/kg) has been shown in two double-blind, placebo-controlled trials to be safe and effective in the treatment of childhood migraine. The first study compared ibuprofen (10 mg/kg) to acetaminophen (15 mg/kg) and placebo. Both ibuprofen and acetaminophen were significantly more effective than placebo in providing pain relief at 2 hours. Differences between ibuprofen compared with acetaminophen were not statistically significant at 2 hours. Acetaminophen was considered effective and well tolerated. In the second study, ibuprofen (7.5 mg/kg) was found to reduce headache severity in children ages 6 to 12 years; however, significant differences at the 2-hour primary endpoint were only demonstrated in boys. No statistically significant adverse effects of ibuprofen or acetaminophen were reported in these studies.[67,68]

The 2004 AAN Practice Parameter has found that "ibuprofen is *effective* and should be considered for the acute treatment of migraine in children." In addition, the parameter concludes that "acetaminophen is *probably effective* and should be considered for the acute treatment of migraine in children."

The "Triptan" agents. The introduction of the 5-hydroxytryptamine (5-HT1) agonists, the "triptans," has revolutionized the treatment of migraine attacks in adults. Multiple controlled trials in adolescents have demonstrated the safety of triptans. Efficacy, however, has only been demonstrated with sumatriptan and zolmitriptan in the nasal spray forms. None of the oral triptans have clearly demonstrated effectiveness in controlled, masked trials and none are approved by the FDA for adolescent use.

Nonetheless, children and adolescents who have not had sufficient relief from acetaminophen, ibuprofen, or naproxen may be candidates for the triptans. In our practice, the most commonly used triptans are sumatriptan nasal spray (20 mg) and tablets (25, 50, 100 mg), zolmitriptan nasal spray (5 mg), and oral disintegrating tablets (2.5, 5 mg), almotriptan tablets (6.25, 12.5 mg), and rizatriptan oral disintegrating tablets (5, 10 mg).

Caution should be exercised with the triptan class if there is a history of hypertension, use of monoamine oxidase inhibitors, basilar or hemiplegic migraine, or family history of early coronary artery disease. A clear contraindication would be any past history of ischemic heart disease.

Sumatriptan. Sumatriptan has been the most rigorously studied "triptan" in adolescents (>12 years). It is available in tablet, nasal spray, and subcutaneous injection form; the oral tablets and nasal formulations are preferable for use in children.

Oral sumatriptan has been studied in a double-blind, placebo-controlled trial of 25-, 50-, and 100-mg tablets in 302 adolescents in 35 sites. Response to sumatriptan met statistical significance when compared with placebo at 25, 50, and 100 mg at the 180- and 240-minute mark showing 74% pain relief at the 4-hour mark; however, the primary endpoint of the study was at 2 hours, and for this timeframe statistical significance was *not* reached.[69]

Common side effects include the feeling of warmth or flushing, chest or jaw tightness, facial burning, stinging, and numbness. Rarely, palpitations, tachyarrhythmias, and hypotension are seen.

Sumatriptan nasal spray studied in three controlled trials has demonstrated both efficacy and safety in adolescent migraine. The first study (n = 14) found significant headache relief at 2 hours in 85.7% versus 42.9% in the placebo group ($P = 0.03$). Headache-associated symptoms were also significantly improved in the sumatriptan group; nausea decreased by 36% and phonophobia decreased by 57%.[70]

The second study was multicenter, double-blind, and placebo-controlled and included 510 adolescents, ages 12 to 17 years, comparing 5, 10, and 20 mg sumatriptan nasal spray to placebo. The 2-hour response rate, defined as reduction in headache severity from severe or moderate to mild or no headache, was 66% for the 5 mg dose ($P < 0.05$), 63% for the 20 mg dose ($P = 0.059$), and 53% for placebo. Significant relief was noted at 1 hour in the 5 and 20 mg dosing arms ($P < 0.05$). A pain-free state at 2 hours was achieved with the 20 mg nasal spray ($P < 0.05$). Both photophobia and phonophobia were reduced with the 20 mg dose ($P < 0.05$). The only adverse effect noted was taste disturbance (26%).[71]

The third trial, a double-blind, placebo-controlled, two-way crossover design (n = 83), included younger children (ages 8 to 17 years) with a median age of 12.4 years. Doses of 10 mg nasal spray were provided for

children weighing 20 to 39 kg and 20 mg for children weighing >40 kg. The primary endpoint was headache relief as defined by a 2-point improvement in headache severity based on a 5-point pain scale at 2 hours. At 2 hours, the primary endpoint was met in 64% of patients receiving sumatriptan and in 39% of those receiving matching placebo ($P = 0.003$). At 1 hour, headache relief was found in 51% of children receiving sumatriptan and in 29% receiving placebo ($P = 0.014$). Complete pain relief was experienced by 31% of those treated with sumatriptan and 19% receiving placebo ($P = 0.14$). Secondary endpoints included the use of rescue medications and patient preference; these results also "favored" sumatriptan (NS). Bad taste was again the most common side effect (29%).[72]

Taste disturbance is the most common problem encountered with sumatriptan nasal spray. One technique to limit the unpleasant taste is to instruct the adolescents in the correct way to administer the nasal spray medication. It is important to "aim" the spray toward the upper nose and to keep the head upright following administration. The patient is coached to avoid "sucking" the medicine back into the oropharynx, where it can be tasted. In addition, the disturbance in taste may be mitigated in many patients by the use of flavored lozenges or hard candy (eg, butterscotch) after administration of the nasal spray. Some migraine sufferers are willing to tolerate the bad taste given the medication's beneficial effects on their headaches.

Overall, sumatriptan nasal spray 20 mg provided the most rapid treatment across this adolescent population group. The 2004 AAN Practice Parameter has found that sumatriptan nasal spray "is effective and should be considered for the acute treatment of migraine in adolescents."

Subcutaneous sumatriptan. One open-label trial of the effectiveness of subcutaneous sumatriptan (0.06 mg/kg) showed an overall efficacy of 72% at 30 minutes and 78% at 2 hours, with a recurrence rate of 6%. Due to the tendency for children to report shorter headache duration, a recurrence rate of 6% would seem appropriate for this study population.[73] The obvious limitation to the use of a subcutaneous preparation is children's aversion to "shots."

Rizatriptan. Rizatriptan (Maxalt) is available in 2.5 and 5 mg tablets and oral disintegrating tablets. A single study of adolescents ages 12 to 17 years (n = 149) in a double-blind, placebo-controlled, parallel-group, single-attack design with 5 mg dosing found "pain relief" at 2 hours for the rizatriptan group was 66%, with a pain relief response of 57% (P = NS) for the placebo group. Of note, the response rate was better on weekends. "Functional disability" was significantly improved with rizatriptan 5 mg (44%) compared with the placebo group (36%). There were no serious adverse events and the most common adverse events reported were fatigue, dizziness, somnolence, dry mouth, and nausea.[74]

Zolmitriptan. Zolmitriptan (Zomig) tablets were studied in adolescents (n = 38) who entered in a 1-year open-label trial. The first two migraine subgroups were treated with 2.5 mg and subsequent attacks with 2.5 or 5 mg at each patient's discretion. The overall headache response at 2 hours was 80% (88 and 70% with zolmitriptan, 2.5 and 5 mg, respectively). Treatment was well tolerated.[75]

A recent clinical trial of zolmitriptan NS (5 mg) used a novel study design in an attempt to mitigate the high placebo response rate seen in previous adolescent trials. Each study subject initially treated a migraine attack with a placebo nasal spray within 30 minutes of the onset of their headache (single-blind phase). If a headache response was obtained at 15 minutes, no further medication was taken. Those patients with ongoing headache of moderate to severe intensity 15 minutes after the first (placebo) spray then took either the active agent or the matched placebo (double-blind phase). Zolmitriptan NS demonstrated a headache response rate at 1-hour post-dose superior to placebo (58.1% versus 43.3%; $P < 0.02$). The onset of action was as early as 15 minutes. The 2-hour sustained headache response rate for zolmitriptan NS was 53.4% versus 36.2% for placebo ($P < 0.01$). Of patients treated with zolmitriptan NS, 51% were able to return to normal activities at 1 hour versus 37.5% treated with placebo ($P < 0.03$). There were no serious adverse events or withdrawals due to adverse events. There was a low incidence of any adverse events, with unusual taste (dysgeusia) being the most common side effect reported (6.5%).[76]

Antiemetics. For many children with migraine, the accompanying symptom of nausea or vomiting can be just as disabling as the pain. Antiemetics, available in suppository, oral, sublingual, or parenteral forms, are extremely useful in children and adolescents with acute migraine accompanied by disabling nausea or vomiting. Commonly used agents are shown in Table 17.

Table 17. Anti-emetics for pediatric migraine

Drug	Dose	Available	Toxicity
Hydroxyzine	10-25 mg bid-tid	Syrup 10 mg/tsp Tabs 25, 50 mg	Sedation
Promethazine	0.25-0.5 mg/kg/dose	Tabs 12.5, 25, 50 mg Syrup 6.25, 12.5 mg/tsp Suppository 12.5, 25, 50 mg	Sedation Dystonic Reactions*
Prochlorperazine	2.5-5 mg bid	Tabs 10, 15 mg Syrup 5 mg/tsp Suppositories 2.5, 5, 25 mg	Sedation Dystonic Reactions
Metoclopromide	1-2 mk/kg (≤10 mg)	Tabs 5, 10 mg Syrup 5 mg/tsp	Sedation Dystonic Reactions
Ondansetron	4-8 mg q 8 hours	4, 8 mg tablet 4, 8 mg oral disintegrating	Sedation Dystonic Reactions

*Oculogyric crisis (managed with IV benadryl).

Preventive Measures. A diverse group of medications including antihistamines, antidepressants, and anticonvulsants have been used to prevent attacks of migraine, but few have demonstrated effectiveness in controlled trials. Their use should be limited to patients whose headaches occur with sufficient frequency or severity as to warrant a daily treatment program. Generally, a minimum of three headaches per month justifies use of a daily prophylactic agent. A clear sense of *functional disability* must be established before committing to a course of daily medication. It is also a good clinical strategy to identify the presence of "comorbid conditions" (eg, depression, obesity) that may suggest the relative benefit of one medicine over another.

The duration of treatment is controversial, but the general practice is to treat through the school year and then to gradually eliminate daily preventive agents during summer vacation. In adult practice, a 6-month course of treatment is often recommended. In young children (~3 to 8 years old), another option is to use a shorter course (eg, 6 to 8 weeks) followed by a slow taper. In recognition of the cyclical nature of migraine, the daily agents should be used for a finite period of time.

From the practice perspective, once the decision is made to institute daily preventive medication, used in tandem with biobehavioral programs, a particular agent is selected based on the individual patient's age, gender, and comorbidities. The recommended course of action is to introduce the medication gradually and monitor its tolerability and the effects on headache frequency, severity, and response to acute treatments. A minimum of 6 to 12 weeks is necessary in most instances to assess the effects. Patience must be exercised! Many patients and their families anticipate immediate responses, so the anticipatory guidance must be given that these medicines take time to achieve their full beneficial effects. The following description of each medicine will provide what little research "evidence" exists along with some practical considerations about their use, based on clinical experience.

While there is an unfortunate lack of controlled data regarding drug therapies for migraine prophylaxis in children, data are beginning to emerge. Use of the many of these agents (Table 18) is based on anecdotal information or extrapolated adult experience.

Antihistamines. ***Cyproheptadine.*** This is an antihistamine with both antiserotonergic and calcium channel blocker properties which is widely used for migraine prevention in young children (generally <12 years of age), but has not been subjected to controlled trials.

One retrospective study of the use of preventative agents for migraine in children and adolescents within one pediatric neurology practice found that headache frequency was reduced from a mean baseline of 8.4 headaches/mo to 3.7 headaches/mo with doses ranging between 2 and 6 mg given at bedtime or divided twice a day. A "positive response rate," defined as an overall favorable decrease in headache frequency and intensity plus acceptability of the agent, was noted in 83% (n = 30). Common side effects included sedation and increased appetite.[77]

Dosing schedules can vary widely from single bedtime schedules to tid regimens. A dose of 2 to 4 mg

Table 18. Preventive medications for pediatric migraine

Drug	Dose	Available	Toxicity
Antihistamines			
Cyproheptadine	0.25-1.5 mg/kg	Syrup 2 mg/tsp Tab 4 mg	Sedation Weight gain
Antidepressants			
Amitriptyline	5-25 mg qhs	Tabs 10, 25, 50 mg	Sedation
Nortriptyline	10-75 mg qhs	Tabs 10, 25, 50, 75 mg	Weight gain
Anticonvulsants			
Topiramate	1-10 mg/kg/day	Sprinkles 15, 25 mg Tablets 25, 100	Sedation Paresthesias Weight loss Glaucoma Kidney stones
Valproic acid	20-40 mg/kg/day (usual 250 mg bid)	Syrup 250 mg/tsp Sprinkles 125 mg Tabs 250, 500 ER† 250, 500	Weight gain Bruising Hair loss Hepatotoxicity Ovarian cysts
Gabapentin	10-40 mg/kg/day	Syrup 250 mg/tsp Tablets 600, 800 mg Capsules 100, 300, 400 mg	Fatigue Ataxia Tinnitus
Anti-hypertensive agents			
Beta-blockers*			
Propranolol	2-4 mg/kg/day	10, 20, 40, 60, 80 mg LA cap 60, 80, 120, 160 mg	Hypotension Sleep disorder Decreased stamina Depression
Metoprolol	2-6 mg/kg/day	Tab 50, 100	Same
Nadolol	0.5-2.5 mg/kg/day	Tab 20, 40, 80 mg	Same
Calcium channel blockers			
Verapamil	4-10 mg/kg/day tid	Tab 40, 80, 120 mg SR tab 120, 180, 240 mg	Hypotension, Nausea AV block Weight gain
Nonsteroidal anti-inflammatory agents			
Naproxen sodium	250-500 bid	Tab 220, 250, 375, 500 mg	Gastric upset

*Avoid when: asthma, diabetes.
†Extended release, once daily preparation.

orally at bedtime is a rational starting point with the option to increase to a maximum of 12 to 16 mg per day divided three times per day. However, doses greater than 8 mg per day often cause excess sedation.

Cyproheptadine has two major limiting features: sedation and appetite stimulation. These effects may restrict its acceptability in adolescence, but may be advantageous in thin preadolescents.

Antidepressants. Antidepressants have become a mainstay of migraine prevention in children and adolescents. There are ample data to support the efficacy of antidepressants for adult migraine.

Two uncontrolled series that studied pediatric and adolescent migraine support the role of *amitriptyline*; no blinded trials exist. The first pediatric study included 192 children with headache, of whom 70% had migraine. The average age was 12 years and the patients had more than three headaches per month. They were treated in an open-label fashion with amitriptyline up to a dose of 1 mg/kg/d. Eighty-four percent reported an overall reduction in headache frequency and severity. Looking specifically at the migraine subset, there was a statistically significant reduction in headache frequency and severity; however, the duration of headache attacks was unchanged when compared with initiation of the drug. Side effects were minimal.[78]

The second study, a retrospective review of the use of preventative agents for children and adolescents within one child neurology practice, found that amitriptyline produced a "positive response rate" of 89% (n = 73). Positive response rate was defined as an overall decrease in headache frequency and intensity plus acceptability of the agent. Headache frequency

was reduced from a mean baseline of 11 to 4.1 headaches per month. The principle side effect was mild sedation.

The tricyclic antidepressants amitriptyline, nortriptyline, and desimpramine are widely employed and selection is generally a matter of personal preference and experience. There are no comparative data.

Amitriptyline is started as a single bedtime dose of 5 to 10 mg and slowly, every 4 to 6 weeks, titrated upward as necessary, toward 25 to 50 mg. Sedation is the primary complication. Advantages of amitriptyline include its low cost and once-a-day schedule, which improves compliance. An electrocardiogram may be warranted if doses in higher ranges (>25 to 50 mg/d) are used.

The selective serotonin reuptake inhibitors may have a role in those children and adolescents with migraine and comorbid anxiety, depression, or obsessive-compulsive disorder. No controlled studies have been performed in children or adolescents. A morning dose of 10 to 20 mg of fluoxetine (Prozac) may be considered in this population, but caution must be exercised given the recent FDA "black box" warning regarding suicide risks in adolescents with this class of antidepressants.

Antiepileptic agents. Topiramate, valproate, levetiracetam, and gabapentin have expanding roles in pediatric migraine. Considering the current views of the pathophysiology of migraine as a primary neuronal event with propagation of "cortical spreading depression" across the cerebral cortex with cortical excitation-depolarization, the anticonvulsants pose a most intriguing role.

Topiramate has shown efficacy in adult migraine prevention. Adult trials using doses of 200 mg/d (divided twice per day) showed a 50% reduction in headache frequency and severity.[79]

One retrospective study assessing the efficacy of topiramate for pediatric headache included 75 children, predominantly patients with chronic daily headache (≥15 headaches per month). Of the 41 who were available for follow-up, average daily doses of 1.4 ± 0.74 mg/kg/d were reached with a headache frequency reduced from 16.5 ± 10 headaches/mo to 11.6 ± 10 headaches/mo ($P < 0.001$). Mean headache severity, duration, and accompanying disability were also reduced. Side effects included cognitive changes (12.5%), weight loss (5.6%), and sensory symptoms (2.8%).[80]

Topiramate also was studied in a population of 162 children ages 6 to 15 years of age in a double-blind, placebo-controlled fashion. Topiramate was initiated at 15 mg/d and titrated over 8 weeks to a dose approximating 2.0 to 3.0 mg/kg/d, or their maximum tolerated dose, whichever was less. The maximum dose allowed was 200 mg/d. The titration phase was followed by a 12-week maintenance phase. Topiramate reduced mean monthly "migraine days" by 2.6 (from a baseline of 5.4 migraine days) compared with a reduction of 1.9 days for the placebo group (from a baseline of 5.5 days/mo) ($P = 0.065$). A greater percentage of patients receiving topiramate (32%) showed 75% reduction in mean monthly migraine days than patients receiving placebo (14%) ($P < 0.020$). The most common adverse events were anorexia (13.0% versus 8.2% placebo), weight decrease (9.3% versus 6.1% placebo), paresthesia (8.3% versus 0.0% placebo), and somnolence (8.3 versus 6.1 placebo).[81]

Divalproex sodium was investigated in a retrospective study of migraine prophylaxis in children ages 7 to 16 years (n = 42) at a dosing range of 15 to 45 mg/kg/d. It was found that 81% of children were successful in discontinuing all acute medications. After 4 months of treatment, 75.8% of the patients reported a 50% reduction in headache frequency; 14.2% had a 75% reduction and 14.2% achieved a headache-free status. Side effects included gastrointestinal upset, weight gain, somnolence, dizziness, and tremor, very similar to those experienced by patients using it in the management of their epilepsy.[82]

A second small study using sodium valproate included children ages 9 to 17 years (n = 10) treated in an open-label fashion with doses between 500 and 1000 mg. Both headache severity and frequency were reduced. Mean severity at baseline using a visual analog scale was reduced from 6.8 to 0.7 at the end of treatment ($P = 0$). Mean headache attacks per month were reduced from 6/mo to 0.7/mo and mean duration of headache attack was reduced from 5.5 hours to 1.1 hours following treatment. Side effects included dizziness, drowsiness, and increased appetite, but no serious side effects were noted in this study. The authors concluded that sodium valproate is safe and effective for migraine prophylaxis in children.[83]

The doses used for valproate are lower than those used for seizure control. A schedule of 10 mg/kg/d or 250 mg po twice per day or a single bedtime dose of the extended release preparation (250 mg, 500 mg) is

a rational starting point. The acceptability of valproate in adolescent females warrants caution in view of the appetite stimulation and risk of ovarian dysfunction (eg, polycystic ovary). A similar monitoring schedule to that used for patients taking valproate for epilepsy applies with periodic measurements of blood counts including platelets, liver chemistries, and amylase.

Levetiracetam at doses of 125 to 250 mg twice daily was assessed in a retrospective fashion in a sample of 19 patients (mean age 12 years) treated for a mean duration of 4.1 months. The average frequency of headache attacks before treatment was 6.3/mo and after treatment fell to 1.7/mo ($P < 0.0001$). A striking 52% of patients experienced "elimination" of migraine attacks during treatment. No side effects were reported in 82.4% but 10.5% discontinued treatment because of side effects including somnolence, dizziness, and irritability.[84] These impressive results suggest a need for a controlled trial.

Gabapentin was reported to be effective in one small retrospective study (n = 18) of children using doses of 15 mg/kg. Over 80% of patients experienced more than 50% reduction in headache frequency and severity.[85] Perhaps the most desirable feature of gabapentin is the low incidence of side effects.

Clearly, more research is needed in children to assess the efficacy and tolerability of antiepileptic agents for migraine prevention.

Antihypertensive agents. ***Beta-blockers.*** Though widely felt to be the "drug of choice" for migraine, *propranolol* has been studied in three randomized, double-blind studies and the results have *failed to consistently* demonstrate effectiveness. While beta-blockers are still viewed as one of the first-line agents in adult migraine, they have a limited role in pediatric and adolescent medicine.

The first study that did demonstrate some effectiveness of propranolol was a double-blind, crossover trial in children ages 7 to 16 years (n = 28) using 60 to 120 mg per day (0.5 to 1 mg/kg/d divided three times per day). Among the propranolol-treated patients, 20 of 28 patients (71%) had complete remission from headaches and another 3 patients (10%) experience a 66% reduction in headache frequency. In the placebo group, 3/28 had complete remission and 1 of the 28 experienced a 66% improvement. The author concluded that propranolol has an "excellent prophylactic effect" for children with frequent and severe attacks of migraine.[86]

A second study (n = 39) failed to demonstrate benefit using slightly higher doses of propranolol (80 to 120 mg/d); in fact, it showed a significant *increase* in the average duration of headache in the propranolol treatment group.[87] A third trial compared propranolol at a dose of 3 mg/kg/d versus self-hypnosis and found no benefit from propranolol but significant improvement with hypnotherapy.[88]

Propranolol may be used on a single daily dose ("LA") form or on a two or three times per day schedule. The LA preparation is most useful. The starting dose is 1 to 2 mg/kg/d and is slowly increased to 3 mg/kg/d as tolerated. Dosing adjustments can be made every 2 to 3 weeks.

Another beta-blocker, *timolol,* was assessed in a randomized crossover trial with 8 weeks in each arm and a 4-week washout period between the arms (n = 19). Headache attacks were reduced from 1.37/wk at baseline to 0.23/wk in the timolol group. In the placebo group, attacks were reduced from 1.06/wk baseline to 0.59/wk. The authors reported no significant beneficial effect from timolol.[89]

The selective beta-blockers *atenolol, metoprolol, and nadolol* are alternative choices, but there are no data to suggest any relative advantage of one versus another.

Beta-blockers as a group are contraindicated in the presence of reactive airway disease, diabetes mellitus, orthostatic hypotension, and certain cardiac disorders associated with bradyarrhthmias. Curiously, however, a subset of patients with neurocardiogenic syncope and comorbid migraine do very well with propranolol.

Special caution must be made about the use of beta-blockers in two other populations: athletes and patients with affective disorders, particularly depressions. Athletes may experience a lack of stamina and decreased performance. Those children with comorbid affective disorders can experience deterioration of mood, even suicidal depression, with propranolol.

Calcium channel blockers. Calcium channel blockers are thought to exert their antimigraine effects by way of selective inhibition of vasoactive substances on cerebrovascular smooth muscle.

Nimodipine (10 to 20 mg three times per day) was studied in a single controlled, crossover trial of children ages 7 to 18 years (n = 37); the results were inconsistent between the two treatment phases. During the first treatment period, there was no difference between the active drug and the placebo. Headache frequency per month fell from 3.3 to 2.8 in the active

group and from 3.0 to 2.5 in the placebo group (n = NS). During the second treatment phase, there was a significant reduction in headache frequency in the nimodipine group, but there was no effect on headache duration. Side effects were limited to mild abdominal discomfort in >1%.[90]

Flunarizine is a remarkable calcium channel blocker that has been evaluated in several well-controlled trials. Two double-blind, placebo-controlled trials using 5 mg bedtime doses of flunarizine (n = 105) demonstrated significant reduction in headache frequency in both studies, one also showing decreased headache duration.[91,92] In this first trial, the number of headaches was reduced from a baseline of 8.66 over 3 months to 2.95 attacks during treatment. Of patients taking flunarizine, 76% noted a ≥50% improvement, whereas only 19% taking placebo had ≥50% improvement. Another open-label trial of 13 patients showed decreased headache frequency.[93] Other than sedation (9.5%) and weight gain (22.2%), side effects were minimal.

Based on these strong data, the 2004 American Academy of Neurology Practice Parameter for the treatment of pediatric migraine found (paradoxically) that "flunarizine is *probably effective* for preventive therapy and can be considered for this purpose but it is not available in the United States."

Nonsteroidal anti-inflammatory agents. Naproxen sodium has been shown to be effective in adolescent migraine in one small series using a double-blind, placebo-controlled crossover design. Sixty percent of the patients experienced a reduction in headache frequency and severity with naproxen 250 mg bid, whereas only 40% responded favorably to placebo. The rate-limiting effect is gastrointestinal discomfort.[49,94] For that reason, use should be limited to about 2 months duration.

Summary of preventive agents. Based on recent review of the medical literature, the calcium channel blocker flunarizine is the only agent that has been studied in rigorous controlled trials and found to be effective.[95] Flunarizine is, however, unavailable in the United States.

There are uncontrolled data to suggest a beneficial effect with the antihistamine cyproheptadine, the antidepressant amitriptyline, the nonsteroidal antiinflammatory agent naproxen, and the anticonvulsant agents topiramate, valproic acid, and gabapentin. There is conflicting controlled evidence regarding propranolol and trazadone. Clonidine, pizotifen, nimodipine, and timolol were not shown to be more effective than placebo.

Table 19. Diagnostic criteria for tension-type headache

Tension-type headache
A. At least 10 episodes fulfilling the criteria B-D
B. Headache lasting 30 minutes to 7 days
C. Headache has at least two of the following characteristics:
   1. Bilateral location
   2. Pressing/tightening (nonpulsating) quality
   3. Mild to moderate intensity
   4. Not aggravated by routine physical activity such as walking or climbing stairs
D. Both of the following:
   1. No nausea or vomiting
   2. No more than one of photophobia or phonophobia
E. Not attributed to another disorder

An excellent Cochrane Database Review (www.cochrane.org) concludes with the statement that there is a "clear and urgent need" for methodologically sound, randomized controlled trials for the use of prophylactic drugs in pediatric migraine.

"Status Migraine". The formal definition of status migraine is persistence of symptoms more than 72 hours. This, in the author's view, is an arbitrary and clinically irrelevant definition. In a more practical sense, any protracted, disabling, and debilitating migraine attack that is intractable to outpatient treatment (ie, oral, sublingual, subcutaneous measures) that requires urgent medical intervention with parenteral agents ought to be the functional definition of status migraine. These patients often present to emergency departments or urgent care clinics for care, and a systematic approach with a series of options must be available.

The five key elements are hydration, analgesia, specific antimigraine agents, antiemetics, and sedation. Table 19 provides a stepwise series of suggestions.

For hydration, intravenous fluids with glucose-containing solutions is imperative. Most patients with status migraine have some degree of dehydration from vomiting or poor oral intake. An intravenous bolus with normal saline or lactated Ringer's solution followed by a 5 to 10% dextrose containing infusion (ie, D5 to 10½ NS) should be started and the patient's volume state monitored, including an evaluation of serum electrolytes and urine.

For analgesia, the options include the "triptan" agents (discussed earlier), ketoralac, and narcotics, although narcotics are discouraged because of the attendant nausea and abuse potential.

The "migraine-specific" regimens include the triptan agents, intravenous valproate (Depacon), or dihydroergotamine (DHE), not used together. Subcutaneous sumatriptan at a dose of 0.06 mg/kg (maximum, 6 mg) is particularly useful in patients intolerant of oral medications. IV valproate, given as a rapid infusion of about 20 mg/kg or a maximum of 1000 mg, though not studied in any controlled fashion, has been reported to have very favorable results.[96]

DHE may be considered for the management of status migraine. Before initiating an IV DHE protocol, it is recommended to give an intravenous antiemetic (eg, metoclopromide). Toxicities of DHE are infrequent, but vomiting can occur. In children and adolescents, the dosing of DHE is important for both efficacy and the limitation of adverse events. DHE, which often needs dose adjustment depending on the patient's age, can be used in the following:

- ages 6 to 9 years, 0.1 mg per dose
- ages 9 to 12 years, 0.2 mg per dose
- ages 12 to 16 years, 0.3 to 0.5 mg per dose[97]

Sedation is often useful, particularly if the first wave of treatment is failing to produce any appreciable impact of the headache. Sleep has wonderful beneficial effects. Diphenhydramine, 25 to 50 mg intravenously, is often quite effective and, when given with the dopaminergic antiemetics, lessens any probability of dystonic reactions. Benzodiazepines have sedative and anxiolytic properties, valuable in status migraine.

Migraine Management Summary

The management of pediatric migraine requires a balance of biobehavioral measures coupled with agents for acute treatment and, if needed, daily preventive medicines. Table 20 provides the migraine management basic sequences. A recent AAN Practice Parameter has critically reviewed the limited data regarding the efficacy and safety of medicines for the acute and preventive therapy of pediatric migraine (www.aan.org).

The first step is to establish the headache frequency and degree to which the migraines impact on lifestyle and performance. The next step is to institute the nonpharmacological measures, such as regulation of sleep (improved sleep hygiene), moderation of caffeine, regular exercise, and identification of provocative influences (eg, stress, foods, social pressures). A wide variety of therapeutic options exist for patients whose migraine headaches occur with sufficient frequency and severity to produce a functional impairment.

Table 20. Establish the migraine diagnosis

Reassurance (that there is no brain tumor causing the headache)
Begin to maintain Headache Calendar
This helps to establish the frequency, associated symptoms, and degree of disability
Bio-behavioral program (guidelines for all migraine patients)
1. Regular sleep schedule
2. Regular eating schedule (no skipping meals, particularly breakfast)
3. Regular exercise (20-30 minutes per day of aerobic exercise)
4. Weight management [if basal metabolic index (BMI) >]
5. Eliminate caffeine
6. Look for and then eliminate defined triggers:
a. Foods
b. Odors
c. Activities
7. Stress management
8. Relaxation therapy
9. Biofeedback
Acute management
Make the medicine *available* where the patient is having their headaches!
Complete necessary school medication forms so the medicine is available at school!
Take the acute medicine *within 20-30 minutes* of the onset of the pain!

Medicine options (see also Table 15)

Age <10 years	Age >10 years
Ibuprofen (7.5-10 mg/kg)	Ibuprofen (400-600 mg)
Acetaminophen (15 mg/kg)	Acetaminophen (325-1000 mg)
Naproxen	Naproxen (250-500 mg)
	Ketoralac (10-20 mg)
	Triptans
	Sumatriptran nasal spray 20 mg
	Zolmitriptan nasal spray 5 mg
	Zolmitriptran oral disintegrating 2.5, 5 mg
	Rizatriptan oral disintegrating 5, 10 mg

Preventive strategies: Medicine options (see also Table 17)

Age <10 years	Age >10 years
Cyproheptadine (2-4 mg q hs*)	Amitriptyline (5-10 mg po q hs up to 1 mg/kg)
Amitriptyline (5-10 mg po q hs)	Topiramate (1-10 mg/kg bid)
Topiramate (1-10 mg/kg bid†)	Valproate (250-500 mg ER po q hs)
Propranolol (2-4 mg/kg bid)	

*q hs = taken orally at bedtime.
†Titrate upward by 15-25 mg every 1-2 weeks toward 5 mg/kg.

The most rigorously studied agents for the acute treatment of migraine are ibuprofen, acetaminophen, and sumatriptan nasal spray, all of which have shown safety and efficacy in controlled trials. For preventive or prophylactic treatment in the population of children and adolescents with frequent, disabling migraine, flunarezine (not available in the U.S.) is the most

efficacious agent, but encouraging data are emerging regarding the use of several antiepileptic agents such as topiramate, disodium valproate, levateracetam, as well as the antihistamine cyproheptadine and the antidepressant amitriptyline.

Daily preventative drug therapies are warranted in about 20 to 30% of young migraine sufferers. The particular drug selected for the individual patient requires an appreciation of other comorbidities such as affective or anxiety disorders, coexistent medical conditions such as asthma or diabetes, and acceptability of potential toxicities such as weight gain, sedation, or tremor. A diverse group including antihistamines, antidepressants, antihypertensives, and anticonvulsants is available (Table 18). Once a particular agent is selected, it should be introduced gradually, given for an adequate time period (usually 4 to 8 weeks), with the duration of treatment clearly defined. Generally, the treatment period is 6 months or until the conclusion of the school year. Younger children can sometime be treated for as brief as 6 to 8 weeks and then taken off their daily preventative agent.

Other Primary Headaches

Tension-type Headache in Children

Epidemiology. Establishing the prevalence of tension-type headache (TTH) in children has proven a challenge. The prevalence estimates range from 11 to 72.8%.[98-102] The largest of these series (n = 8255) that included school children ages 13 to 15 years found a 1-year prevalence of TTH was 18%, while migraine, in this series, had a 1-year prevalence of 7%.

Clinical Features. The ICHD diagnostic criteria for TTH are shown in Table 19. The key element of these criteria is the *absence* of the following migrainous features: unilaterality, pulsing quality, severe intensity, aggravation by activity, nausea or vomiting, as well as photophobia *and* phonophobia. Essentially, these criteria describe a recurring pattern (≥10 episodes) of nonmigrainous headache as being the diagnostic criteria for tension-type headache.

The 2004 ICHD has divided TTH into the following:

Infrequent episodic tension-type headache
Frequent episodic tension-type headache
Chronic tension-type headache

The distinction between infrequent, frequent, and chronic relates to the number of headaches per month: *infrequent*, less than one per month; *frequent*, more than one per month but not more than 15 per month; and *chronic*, more than 15 per month. In Gallai's series of 244 children with TTH it was determined that 52% of these headaches were episodic, 16% were chronic, and 33% had TTH that did not fulfill criteria for either.[103]

Children and adolescents who suffer from tension-type headaches report similar symptoms as adults, with some slight modifications.[104-106] The *duration* of attacks may vary from 5 to 30 minutes or last greater than 48 hours. Gallai identified that, in 36.7% of children with tension-type headache, these lasted less than 30 minutes. The *location* of headache is often difficult for young children to describe.[107] Bilateral location was identified in 57 to 86% of patients. Wober-Bingol and colleagues observed that adolescents more often fulfill the criterion for location than younger children. The *quality* of headache was most often described as pressing or tightening (74%) rather than pulsating (16%). In one series, only 15% of children described exacerbation with routine physical activity. Seventy-five percent described the headache as mild to moderate intensity. The *intensity* is probably the most relevant headache characteristic for differentiating TTH from migraine. Children with TTH are less likely to report abdominal pain, nausea, vomiting, vertigo, visual disturbances, sweating, vomiting, or using a darkened room for pain relief (9 to 30%).

Therefore, the "nonmigraine" features of quality (pressing or tightening), intensity (mild-moderate), and lack of associated symptoms may be more specific for TTH headache (versus migraine) than location or duration in the pediatric population. Clearly, large, prospective series are needed.

Management. There are only two published trials investigating the pharmacological management of tension-type headache in children or adolescents.

One clinical trial compares relaxation training ("limited contact format") compared with amitriptyline (10 mg daily) for children ages 8 to 16 years (n = 19) for 3 months. Clinical improvement was observed in both groups. For the amitriptyline-treated group, baseline headaches were 17 ± 11 migraines/mo and reduced to 5.6 ± 6.7 headaches per month following 3 months. This is comparable to the behavioral group where baseline was 12.1 ± 10.1 headaches/mo down to 6.4 ± 9.6 per month (P = NS).[108]

The second trial (n = 48) compared the efficacy of relaxation to a muscle relaxant chlormezanone in the

treatment of adolescent TTH in a randomized, double-blind, crossover design and found significant improvement in the home-based relaxation therapy *without* further improvement with the addition of drug treatment.[109]

Biobehavioral therapies (eg, relaxation treatment and thermal biofeedback) have been assessed. Two studies comparing relaxation therapy for adolescents with migraine, migraine plus TTH, or TTH alone found significant improvement in the migraine population but not the TTH group.[110,111] A study of 37 children, whose average age was 12, with episodic TTH were seen in small group settings once per week for 8 weeks and taught coping skills and progressive relaxation techniques. Statistically significant and sustained (~1 year) reduction in headache days, "state and trait" anxiety, and depression scales were reported.[112] Another study of five children, ages 8 to 14 years, with TTH used six sessions of thermal biofeedback and found significant reduction in headache frequency, duration, and intensity with sustained (6-month) headache-free state in four of the five children.[113] A combination approach with electromyogram biofeedback and progressive muscle relaxation therapy found improvement in headache parameters in 86% of patients versus improvement of 50% of the control group, with sustained efficacy for 6 and 12 months.[114]

Prognosis. There is a paucity of information regarding the prognosis of TTH in children. No longitudinal series have been published. Comorbidity has been evaluated. There is a higher frequency of depressive symptoms in children with TTH and they are at increased risk for both headache and psychiatric symptoms as they enter adult life.[115,116]

Chronic Daily Headache

Many adolescents will report the presence of headache virtually every single day. Chronic, nonprogressive, unremitting, daily, or near daily, pattern of headache represents one of the most difficult subsets of headache known as chronic daily headache (CDH). CDH is formally defined as greater than 4 months during which the patient has greater than 15 headaches per month with the headaches lasting more than 4 hours per day. The estimated prevalence of CDH in adolescents is about 1% and may be as high as 4% in the adult population.[117-119] CDH is very common in referral headache clinics, where up to 15 to 20% of patients will present with daily or near-daily head pain.[120]

Understandably, the quality of life of patients with CDH is significantly affected. The negative impact extends beyond the affected patient to their family, friends, and society as a whole. The extensive disability that results from CDH can be measured in school absence, abstinence from after-school activities, and family discord that invariably results. Therefore early diagnosis and management of frequent or chronic daily headaches is essential.

There are four chronic headache categories: chronic migraine, chronic tension-type, new daily persistent headache, and hemicranium continuum. Chronic migraine and chronic tension-type headaches usually evolve from episodic migraine or TTH. The "new daily persistent" headaches appeared to represent a unique entity in which the headache starts quite abruptly without any history of previous headache syndrome but persists for weeks or months. Hemicrania continua is uncommon in children and represents a cluster variant with daily or continuous unilateral pain with conjunctival injection, lacrimation, rhinorrea, and, occasionally, ptosis. One of the key features of hemicrania continua is responsiveness to indomethacin.

Each of these four types of CDH is further separated into those with or those without superimposed analgesic overuse. The medications implicated in this analgesic overuse syndrome include most over-the-counter analgesics (acetaminophen, aspirin, ibuprofen), decongestants, opioids, butalbital, isometheptene, benzodiazepines, ergotamine, and triptans.[121]

The management of CDH is difficult, but breaking the cycle of daily headaches is the principle goal. Pharmacological efforts, used in isolation, will be uniformly unsuccessful. Therefore, initiation of a multi-disciplined approach with emphasis on preventive strategies takes precedence over the use of intermittent analgesics. This population of patients has already likely been overusing over-the-counter analgesic agents, so a fundamental change in treatment philosophy must be taught to the patient and their family.

The first part of this teaching process must be the incorporation of lifestyle changes, such as regulation of sleep and eating habits, regular exercise, identification of triggering factors, stress management, biofeedback-assisted relaxation therapy, and biobehavioral

Table 21. Cluster headache and the trigeminal autonomic cephalalgias

Key clinical features:	Cluster	Paroxysmal Hemicrania	SUNCT*
Number of attacks	5	20	20
Location of pain	Unilateral Orbital Supraorbital	Unilateral Orbital Supraorbital	Unilateral Orbital Supraorbital
Duration of attacks	15-180 minutes	2-30 minutes	5-240 seconds
Frequency of attacks	qod-8/day	5/day	3-200/day
Autonomic symptoms†	CI, L, NC, R, EE, FS, M, P, Restlessness Agitation	CI, L, NC, EE, FS, M, P	CI, L
Indomethicin response	Negative	Positive	Negative
Occurrence in children	++	+++	2 reported

*SUNCT, short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing.
†Autonomic symptoms: CI, conjunctival injection; L, lacrimation; NC, nasal conjestion; R, rhinorrhea; EE, eyelid edema; FS, forehead or facial sweating; M, miosis; P, ptosis.

programs with psychological or psychiatric intervention.

Lifestyle changes include five major components:

1. Return to the routine of adolescent "life"
2. Adequate and regular sleep
3. Regular exercise (20 to 30 minutes per day of aerobic exercise)
4. Balanced nutrition, including avoidance of skipping meals,
5. Adequate fluid intake with avoidance of caffeine

The pharmacological treatment of chronic daily headaches requires an individually tailored regimen with the judicious use of appropriate prophylactic and analgesic agents. Recognizing the degree of disability will help guide the aggressiveness of the management.

Preventive therapies used for CDH include tricyclic antidepressants (amitriptyline), antiepileptic agents (eg, topiramate, disodium valproate, gabapentin), beta-blockers (propranolol), calcium channel blockers, and NSAIDs.

When making the choice of drug, it is important to consider comorbid conditions. For the patient with difficulty falling asleep, amitriptyline at bedtime may provide dual benefits. Similarly, if there are mild to moderate affective issues, amitriptyline, valproic acid, or one of the selective serotonin reuptake inhibitors may be beneficial. If there is comorbid obesity, topiramate may decrease the appetite. Alternatively, if the patient's appetite is low, valproate often stimulates the appetite. The doses used are shown in Table 18.

The use of analgesic agents for adolescents with CDH is difficult since most of the children describe continuous or near-continuous pain. When do you give the acute analgesic and how do you avoid analgesic overuse? One approach is to graph the pattern of headaches to identify the periods of intense headache, as it stands out from the background pain. At this time, analgesics, including the "triptan agents," may be most useful. The key to effective use of analgesic in the CDH population is for the patient to recognize the migraine component of the headache as soon as it starts, use an adequate dose, and avoid overuse.

The natural history and outcome of CDH is poorly understood. One report provides short-term follow-up on 24 adolescents with CDH, with a peak age of 13 years, for whom greater than half experienced a >75% reduction in headache frequency and one-third experienced a >90% improvement in a 6-month follow-up. A wide variety of preventive agents were employed, but amitriptyline and topiramate provided the largest proportion of successful outcomes.

Cluster and the Trigeminal Autonomic Cephalalgias (TACs)

Cluster headache and the "TACs" are very uncommon in children. Clinically, these entities share the clinical features of repetitive attacks of intense headache accompanied by prominent cranial *parasympathetic signs and symptoms*.. The common pathophysiology relates to the activation of the "trigeminal-parasympathetic reflex." Table 21 compares and contrasts the clinical features.

Cluster. Cluster headache is an uncommon primary headache with an estimated prevalence of 0.1 to 0.9% of the general population. Reports indicate the onset of cluster headaches occurs between 20 and 50 years of

age and has a slight male predominance.[122] Information regarding cluster headaches in children is limited, but the estimated prevalence of childhood onset of cluster is 0.1%.. One large series found the prevalence of cluster in 18-year-old men to be 0.09%.[123] Another series of 35 patients with onset of cluster headache before age 18 years found that 7/35 experienced the onset of symptoms before age 10. Long-term follow-up revealed that 14/35 had gradually increasing frequency and duration of their symptoms through adult life.[124]

The pain of cluster is described as excruciating and boring and is strictly unilateral, located in the temporal and periorbital regions. In contrast to migraine headaches, cluster headaches do not become bilateral nor do they switch sides during an attack, but the pain may occur on opposite sides with different cycles. Many experience autonomic features such as ipsilateral rhinorrhea, tearing, and nasal congestion.[125] Attacks are relatively brief, lasting from 15 minutes to 3 hours.

Most patients experience one to several attacks per day occurring in cycles or clusters that last from weeks to months followed by spontaneous pain-free periods that last from 6 months to 2 years. Cluster headaches may also have circadian and circannual components. Many report headaches often occur at night or toward the end of a sleep cycle.[126]

The management of cluster headaches is divided into acute measures and preventative strategies but there are no published reports of the treatment of cluster in children or adolescents.

A wide variety of treatments are proposed for the treatment of cluster headache that include oxygen (100% at 8 to 10 L/min for 15 minutes), lidocaine (4% aqueous drops intranasally), olanzapine (2.5 to 10 mg orally at onset), dihydroergotamine (1 mg IV, SC, or IM at onset with repeated doses), or sumatriptan (6 mg subcutaneous at onset). Inhaled 100% oxygen has proven to be a successful abortive treatment; however, access to this therapy poses clear limitations in its use. For adults, there is controlled, masked data (Class I) demonstrating efficacy of subcutaneous sumatriptan acute relief of cluster headache.[122-124,127]

Because an attack may occur repeatedly for weeks to months, suppressive or preventative therapies are essential to the management of cluster headache. Corticosteroids (prednisone 40 mg/d for a 3- to 5-day pulse followed by 3-week taper) are valuable because they may rapidly suppress an attack. Other options include the following: ergotamine tartrate (2 mg qhs), sumatriptan (100 mg tid for up to 7 days), naratriptan (2.5 mg bid for 7 days), lithium (300 mg bid-qid), verapamil (80 to 240 mg tid), sodium valproate (250 to 1000 mg bid), topiramate (25 to 200 mg bid), or melatonin (10 mg daily). Prednisone is the most commonly employed agent for short-term pulses to suppress attacks. Verapamil may be the most commonly used agent for maintenance preventive therapy. Histamine "desensitization" and/or combination approaches are utilized for patients with refractory symptoms and, infrequently, surgical ablation may be indicated for medically intractable patients.[122-124]

Paroxysmal Hemicrania (PH). PH is an uncommon headache syndrome characterized by brief (2 to 45 minute), intense attacks of unilateral supra- or periorbital pain. The attacks may occur as often as 5 to 30 times per day. The prevalence of PH is only 0.021% and generally begins in adulthood with onset generally in the third decade of life, so this is rare in children.[128] Like other TACs, paroxysmal hemicrania is associated with autonomic symptoms such as tearing, conjunctival injection, rhinorrhea, ptosis, and eyelid edema. A key element defining paroxysmal hemicranias is their *exquisite sensitivity to indomethacin*. This disorder can therefore be distinguished from cluster headaches by their shorter duration, higher frequency, female predominance, and clear response to indomethacin.[129]

Relatively few pediatric cases have been reported in the literature. Children as young as 3 years of age have been described with the disorder. Shabbir and McAbee reported two teenaged girls (13 and 14 years) with chronic PH (symptoms >1 year) with repetitive attacks (8/d) of lancinating unilateral pain without mention of autonomic symptoms, both of whom had partial response to indomethacin, but achieved "nearly complete" relief with verapamil.[130] Gladstein and colleagues reported an 8-year-old boy with typical features of CPH who responded to indomethacin and was symptom free for 1 year.[131]

This author follows three adolescents, all males, with PH. All had episodes of brief, excruciating, disabling attacks of retrobulbar pain with at least one autonomic component and all responded immediately to indomethacin at a dose of 25 mg orally twice a day. One patient stopped the medicine after 2 months and attacks recurred within 1 week.

Short-Lasting Unilateral Neuralgiform Headache Attacks with Conjunctival Injection and Tearing (SUNCT). First described in 1978, SUNCT is an uncommon TAC described in only ~50 complete case

reports and series, overwhelmingly in adults.[132-134] There is a high variability in the frequency of attacks which begin abruptly and last from 5 to 250 seconds.[135] The pain is unilateral in the distribution of the trigeminal nerve particularly around the orbital, periorbital, and temporal region. Patients may have up to 30 attacks per hour, although most report around five to six episodes per hour. As the name implies, the most notable autonomic feature of SUNCT syndrome is the conjunctival injection and tearing. Other concomitant features include rhinorrhea and forehead sweating.

Unlike paroxysmal hemicrania, SUNCT syndrome is unresponsive to indomethacin, and neither oxygen nor other NSAIDS provide relief. While many therapies that are used to treat other short-lasting headaches are ineffective with SUNCT syndrome, partial or complete success has been achieved with sumatriptan and some anticonvulsants (eg, lamotrigine, gabapentin, topiramate, carbamazepine). As with other short-lasting headaches, the prognosis of SUNCT syndrome is poorly understood.

Case reports in children are very rare. Blatter and coworkers described "symptomatic SUNCT" in an 11-year-old girl with right-sided paroxysmal headaches associated with marked autonomic activation. The symptoms began following a febrile upper respiratory tract infection. The patient described the pain as moderate to severe, located at the retromandibular fossa with radiation to the cheek, with up to 20 attacks a day, and each episode lasted from 30 to 60 seconds. The pain was always associated with conjunctival injection, tearing of the right eye, and salivation. She denied photophobia and rhinorrhea. A trial of indomethacin decreased the frequency of attacks from 20 to 10 per day; however, the intensity of the pain remained unchanged. An MRI revealed a mass lesion of the right cerebellum near the entry zone of the right trigeminal nerve root. An exploratory operation showed a growing tumor with prominent vascularization that was histologically identified as a pilocytic astrocytoma. Subtotal removal of the mass resulted in shorter and less intense pain attacks.[136] The presence of any of the TACs in childhood or adolescent should prompt an exhaustive investigation for an organic basis.

Cranial Neuralgias

Uncommon in children, the group of cranial neuralgias is characterized by brief attacks of excruciating pain localized to a particular anatomic distribution (eg, cranial nerve). The diagnostic criteria for each are shown in Table 22. All represent diagnoses of exclusion since neoplastic, demyelinating, structural (ie, Chiari malformation), or inflammatory processes within the contents of the posterior fossa may produce identical symptoms. Ophthalmoplegic migraine has recently been added to the group of cranial neuralgias and was discussed in earlier sections.

Table 22. The cranial neuralgias

Occipital neuralgia
- A. Paroxsmal stabbing pain with or without persistent aching between paroxysms, in the distribution of the greater, lesser, or third occipital nerves
- B. Tenderness over the affected nerve
- C. Pain is eased temporarily by local anesthetic block of the nerve

Trigeminal neuralgia
- A. Paroxysmal attacks of pain lasting from a fraction of a second to 2 minutes, affecting one or more divisions of the trigeminal nerve and fulfilling criteria B and C
- B. Pain has at least one of the following characteristics:
  1. Intense, sharp, superficial, or stabbing
  2. Precipitated from trigger areas or by trigger factors
- C. Attacks are stereotyped in the individual patient

Glossopharyngeal neuralgia (GN)
- A. Paroxysmal attacks of facial pain lasting from a fraction of a second up to 2 minutes and fulfilling B and C
- B. Pain has all the following characteristics:
  a. Unilateral location
  b. Distribution within the posterior part of the tongue, tonsillar fossa, pharynx, or beneath the angle of the jaw or ear
  c. Sharp, stabbing pain
  d. Precipitated by swallowing, chewing, talking, coughing, or yawning
- C. Attacks are stereotyped in the individual patient
- D. There is no clinically evident neurological disorder

Neck-Tongue Syndrome (NTS)
- A. Pain lasting seconds or minutes, with or without simultaneous dysesthesia, in the area of distribution of the lingual nerve and second cervical root and fulfilling B and C
- B. Onset of pain is acute
- D. Pain is commonly precipitated by sudden turning of the head

Occipital Neuralgia (ON). Not uncommon in children, ON is characterized by intense, jabbing painful episodes localized to the distribution of the greater or lesser occipital nerve in the occipital region. An emergency department (ED)-based study identified 12 patients with ON whose symptoms, in addition to occipital pain, included visual disturbances (76%), dizziness (50%), nausea (42%), scalp paresthesias (33%), and tinnitus (33%). In this study, 80% of the patients experienced "significant relief" with local anesthetic injection.[137]

There is only one case series in children and adolescents and it is from the pre-CAT scan era.[138] Care

must be taken to exclude anatomic abnormalities of the upper cervical region and posterior fossa.

Trigeminal Neuralgia (TGN). Also known as "Tic douloureaux," TGN is characterized by very brief, shock-like pain limited to one or more distributions of the trigeminal nerve, but not crossing the midline. The most commonly affected single division is the mandibular branch. The pain is commonly precipitated by trivial stimuli such as washing, shaving, talking, or tooth brushing. The pain may occur spontaneously and may cause a spasm ("tic-like") of the adjacent facial muscles.

TGN occurs in about 1 in 25,000 in the general population and is uncommon before the third decade, with only 1% of the cases occurring before 20 years of age. The medical management of choice is carbamazepine but surgical decompression may be necessary in selected instances.[139] A high proportion of TGN in childhood is associated with defined organic pathology.[140-144]

Glossopharyngeal Neuralgia (GN). This neuralgia is characterized by intense attacks of pain in the sensory distribution of the auricular and pharyngeal branches of the vagus nerve: the ear, base of the tongue, tonsils, or angle of the jaw. Common precipitants include swallowing, coughing, or talking.

GN is generally a milder disease than the other cranial neuralgias with isolated, single attacks being common and the annual recurrence rate for second episodes being low at 3.6%. The annual incidence of GN is 0.7/100,000. There is extensive literature regarding cardiac syncope in association with GN due to the close anatomic relationship between cranial nerves IX and X (vagus) as they exit through the jugular foramen.[145]

Five references of GN in children were found. One described a 13-year-old girl with GN who presented with episodes of paroxysmal pain in the right ear from infancy. MRA revealed a prominent, looping, right posterior inferior cerebellar artery, compressing the right glossopharyngeal and vagal nerve complex at its exit from the medulla.[146] Another report describes GN following amygdalectomy or tonsillectomy.[147] A third report found an association with Chiari I malformation.[148,149] "Otalgic" GN in a 13-year-old boy was refractory to medical management and required cervical section of the glossopharyngeal nerve and its tympanic branch to provide complete relief of symptoms.[150]

Neck-Tongue Syndrome (NTS). Neck-tongue syndrome is related to occipital neuralgia. NTS is an unusual clinical entity, characterized by brief episodes of intense upper cervical or occipital pain accompanied by ipsilateral numbness of the tongue *precipitated* by movement or rotation of the head. The attacks are *brief, stabbing* pain, lasting only seconds up to 1 minute, located unilaterally in the upper neck or occipital region. They are accompanied by transient paresthesias or *numbness of the tongue*, ipsilateral to the pain, and may include lingual "pseudoathetosis," dysarthria, and lingual paralysis. The proposed mechanism is thought to be related to irritation of C2-3 root, with tongue involvement due to afferent impulses traveling from the lingual nerve via hypoglossal nerve to C2 root.[151]

Nearly 25 children and adolescents (ages 8 to 15 years) have been reported with NTS. The majority of children (79%) have no identifiable anatomical abnormalities, whereas about two-thirds of adults with NTS have cervical abnormalities such as ankylosing spondylosis, degenerative disc disease, or osteoarthritis. A benign, familial (autosomal-dominant pattern) has been seen in about five pedigrees.

Once structural pathology is excluded, the management of NTS includes conservative treatments with avoidance of trauma coupled with NSAIDs and, if necessary, agents (eg, carbamazepine, gabapentin) to limit neuropathic pain.

Primary Headache Summary. While migraine and the various forms of chronic daily headache are the most frequent headache syndromes referred for neurological consultation, other primary headache syndromes may begin in the pediatric years. Tension-type headaches are mild to moderate in intensity, often frontal in location, last from minutes to hours, and lack the autonomic and disabling features of migraine. The diagnosis may be made on clinical grounds. Behavioral measures and simple analgesics may be the most useful therapies, though no masked, controlled trials have been reported.

The majority of the "other" primary headaches and cranial neuralgias are brief attacks, with or without autonomic components. Some have characteristic periodicity (eg, cluster and TACs), clear precipitating phenomena (eg, activity, cold, head turning, cough, awakening), and others have specific locations (eg, occipital, oropharyngeal). Some have dramatic, near-diagnostic, responsiveness to indomethicin (eg, paroxysmal hemicrania). Since these "other" entities are

Table 23. ICHD classification of secondary headaches attributed to:

Head and/neck trauma
Cranial or cervical vascular disorder
Nonvascular intracranial disorder
Substance or withdrawal from substances
Infection
Disorders of homeostasis
Disorders of the cranium, neck, eyes, ears, nose, sinuses, teeth, or other facial or cranial structures
Psychiatric disorders

uncommon and may be symptomatic of underlying organic pathology, ancillary diagnostic testing may be considered.

Secondary Headaches

The 2004 ICHD classifies the "secondary headache disorders" into headaches attributed to the factors shown in Table 23. Clinically, for the practicing pediatrician, it is more useful to divide the secondary headaches into the five temporal patterns shown in Table 2.

Acute Headaches

Nontraumatic. The acute or sudden onset of an intense headache immediately raises the question of intracranial hemorrhage from a ruptured or leaking aneurysm or vascular malformation. While uncommon in children, subarachnoid hemorrhages do occur, particularly in those with risk factors such as a coagulopathy, sickle cell disease, or hypertension. Children with cystic kidney disease or coarctation of the aorta have an increase risk for intracranial aneurysms. Familial cavernous angiomas are among the more common identifiable causes of intracranial hemorrhage. The hyperacute development of intense headache accompanied by neck stiffness, alteration of mental status, or focal neurological signs justifies an urgent noncontrasted CT scan of the head.

The majority of acute, nontraumatic, headaches in children, however, are due to self-limited, medically remediable conditions such as upper respiratory tract infections with fever, sinusitis, or migraine (Tables 24 and 25). In Pediatric ED-based studies of acute headache, all of the children with serious underlying conditions (eg, intracranial hemorrhage, brain tumors, meningitis) had objective findings on neurological examination: alteration of consciousness, nuchal rigidity, papilledema, abnormal eye movements, ataxia, or hemiparesis.[152,153] Therefore, abnormality on neurological examination is the principle indication for neuro-imaging.

Table 24. Causes of acute headache in children

Fever
Upper respiratory tract infection (with or without fever)
Sinusitis
Pharyngitis
Meningitis: viral or bacterial
Migraine
Hypertension
Substance abuse: cocaine
Medication: eg, sympathomimetics (methylphenydate), oral contraceptives, steroids
Intoxications: lead, carbon monoxide
Ventriculoperitoneal shunt malfunction
Brain tumor
Hydrocephalus
Subarachnoid hemorrhage
Intracranial hemorrhage

Table 25. Differential diagnosis for chronic progressive headache

Hydrocephalus
Subdural hematoma
Chronic meningitis
Tumor
Abscess
Vascular anomaly
Intoxication (eg, lead poisoning)
Idiopathic intracranial hypertension (pseudotumor cerebri)

A *hyperacute* presentation strongly points toward a vascular disorder such as a hemorrhage due to processes like arteriovenous malformation, capillary angioma, cavernous angioma, venous angioma, or telangiectasia. The differential diagnosis must also include aneurysmal hemorrhage, thrombotic stroke, hemorrhage into an occult tumor, and arterial dissection. Extracerebral hemorrhages (subdural or epidural) can occur with head injury during competition. Hypertensive encephalopathy or hemorrhage can also present in this catastrophic fashion. Sympathomimetic intoxication is an unfortunate reality in society as young athletes attempt to enhance their performance with drugs.

The most important neuro-diagnostic tool in the evaluation of acute headache is a careful history that explores the onset, pace, and evolution of the symptom complex. This will dictate the scope and urgency of ancillary testing.

Posttraumatic Headache. Headache following closed head injury or neck trauma in children is one of the most common secondary headache syndromes. Posttraumatic headache (PTH) is divided into *acute* and *chronic* patterns based on duration of symptoms: less than 3 months duration is considered "acute

PTH," and greater than 3 months considered "chronic PTH."

Acute PTH must immediately raise concerns for traumatic brain injury such as cerebral hematoma (subdural or epidural), subarachnoid hemorrhage, cerebral contusion, or skull fracture. These warrant urgent neuro-imaging, particularly if associated with alteration of consciousness, seizures, or a Glascow Coma Scale <13. Cerebrospinal fluid leaks following meningeal tears can lead to positional or "low-pressure" headaches.

Epidural hematoma is associated with the classic history of the rapid deterioration of mental status following head trauma in the temporal-parietal region of the skull. Damage or tear of the middle meningeal artery produces arterial bleeding into the potential space between the inner side of the skull and the dura mater. The headache is very severe and caused by the tearing and peeling of the dura away from the inner skull. As the blood accumulates rapidly under arterial pressure and the volume of the hematoma increases, there is a progressive decline in mental status following a 15- to 60-minute period of lucidity. As the hematoma expands, the temporal lobe is shifted across the tentorial edge and the third cranial nerve is compressed, sometimes contralateral to the hematoma. Decerebrate or decorticate posturing are ominous signs and indicate compromise of the deeper brain structures, including the brain stem. Emergent neuroimaging is essential along with immediate neurosurgical intervention.

The headache of a subdural hematoma generally follows a subacute or even a chronic progressive pattern accompanied by signs of increased intracranial pressure. Subdural hematomas most commonly occur following trauma but can be found in hypocoagulable states (hemophilia, von Willebrand's disease, thrombocytopenia), sickle cell disease, and in children with cerebral atrophy (microcephaly or medication-induced).

Headache following head injury, in the absence of hematoma, may arise within hours or up to a week following the head injury and the clinical manifestations are quite variable. "Footballer's" migraine may occur immediately following a relatively minor headache that occurs playing sports such as soccer or football and may happen following accidental head injury. The clinical features are confusion, language disorders, and agitation ("confusional migraine").

Chronic PTH may be part of a global postconcussive syndrome with behavioral changes (eg, hyperactivity, hypoactivity), dizziness, tinnitus, vertigo, blurred vision, memory changes, sleep disorder, irritability, or attentional disorders. The duration of symptoms is variable with some patients having brief, self-limited syndromes, while others suffer from headaches for greater than 6 to 12 months. One retrospective study of 23 children with chronic posttraumatic headache found a mean duration of 13.3 months (range 2 to 60 months, median 7 months).[154] The headache forms span the spectrum from tension-type, migraine, chronic daily headache, neuralgias (eg, occipital neuralgia), temporomandibular joint, and even, on rare occasions, cluster headache.

Many athletes competing in contact sports will experience PTH as part of a post concussion syndrome. A common question regards when it is safe to return to full contact. Two organizations, the AAN and the American College of Sports Medicine, have provided guidelines regarding return to activities ranging from 1 to 4 weeks.[155,156] Both organizations have these guidelines available online.

The management of PTH requires an appreciation of the degree of disability produced by the headache. Posttraumatic tension-type headaches can generally be managed with nonsteroidal antiinflammatory agents such as ibuprofen or naproxen sodium. Posttraumatic migraine is treated as discussed earlier with a balance of analgesic or "triptan" agents and, if warranted, daily preventive therapies. For patients with frequent or daily headaches, the same management strategies discussed in the chronic daily headache discussion apply with daily preventive programs; pharmacological, nonpharmacological, and analgesics are appropriate for episodes of intense pain.

There are no outcome data on PTH in children and adolescents, but typically, 3 to 6 months is the anticipated course of recovery. Pending litigation may exacerbate stress levels and contribute to prolongation of the headache syndrome.

Acute-Recurrent. Acute-recurrent headaches imply a pattern of attacks of head pain separated by symptom-free intervals. Primary headache syndromes such as migraine or tension-type headache cause the overwhelming majority of headaches within this pattern. On occasion, recurrent headaches are attributed to epileptic syndromes (eg, benign occipital epilepsy), substance abuse, or recurrent trauma. Rarely, metabolic conditions such as mitochondrial encephalomy-

Table 26. Chronic progressive headache *key* points

Chronic-progressive headaches strongly suggest organic pathology
There is no invariable "brain tumor headache" profile
Key *symptoms:*
Nocturnal or
Morning headache
Nocturnal or morning vomiting
Aggravation by Valsalva maneuver or exertion
Seizures
Neurocutaneous syndromes
Key signs:
Papilledema
Cranial nerve palsies
Ataxia
Focal signs, motor or sensory

opathy, lactic acidosis, and stroke-like attacks (MELAS) may have recurrent migraine-like headaches as a component of the clinical picture. MELAS is caused by a point mutation on the circular mitochondrial DNA ($tRNA^{Leu\ UUR}$).

Chronic Progressive. The chronic progressive pattern is the most ominous of the five temporal profiles and carries with it the greatest likelihood of organic pathology (Table 26). Several associated historical clues may further heighten the chances of increased intracranial pressure. *Morning headache* or headaches *which awaken the child from sleep* are a classic symptom of the dependent edema of intracranial lesions. Likewise, *nocturnal or morning emesis*, with or without headache, suggests increased intracranial pressure and these are particularly common symptoms of tumors arising near the floor of the 4th ventricle. Between headaches, behavioral or mood changes, some of which may be subtle, are described by parents. Cognitive changes, such as declining school performance, can on occasion be the presenting complaint. Careful history can uncover these associated features.

Physical examination in the child with chronic progressive headaches must take into consideration that the majority of brain tumors in childhood are *midline* processes (eg, medulloblastoma, cerebellar astrocytoma, ependymoma, pineal region tumors, craniopharyngioma); therefore, there may be little in the way of "lateralizing" neurological findings. The five key features are papilledema, abnormal eye movements, pronator drift, abnormal deep tendon reflexes, and inability to perform tandem gait (tightrope walking). Examination should also include the skin, looking for neurocutaneous markers.

Patients with neurocutaneous syndromes warrant special mention because these patients are particularly prone to develop intracranial tumors due, at least in part, to the absence of the tumor suppressor genes (ie, neurofibromin). Children with neurofibromatosis type 1 are most likely to develop optic gliomas, although virtually any primary CNS neoplasm, even those uncommon in children such as meningiomas, is more likely. NF type 2 maps to chromosome 22 and also involves the absence of a tumor suppressor gene. The primary CNS tumor among this group of patients is an acoustic schwannoma (acoustic neuroma); these are often bilateral. Children with tuberous sclerosis may develop subependymal giant cell astrocytomas. Other rarer neurocutaneous syndromes such as Von Hipple–Lindau have high associations with CNS tumors such as hemangioblastoma.

It must be remembered that there is no invariable "brain tumor headache." It is essential to recognize this temporal pattern of an escalating headache frequency and worsening severity, which then dictates a course of action, usually, neuro-imaging with an MRI.

In this clinical situation of chronic progressive headache with signs of increased pressure (ie, papilledema), the neuro-imaging may *not* demonstrate focal pathology (ie, tumor, abscess, hematoma). Idiopathic intracranial hypertension (pseudotumor cerebri) would be the most likely condition, but the differential diagnosis must include chronic meningitis (TB, fungi, syphilis, or Lyme disease), intoxications (lead or other heavy metals), and chronic carbon monoxide poisoning. A chronic meningitis picture can also be seen with CNS leukemia/lymphoma or leptomeningeal metastasis. Uncontrolled hypertension can lead to optic disc changes with headache. Chronic sinusitis or venous sinus thrombosis can also produce a pattern of slowly increasing intracranial pressure with normal CT scan.

Lumbar puncture must be considered in this situation and, not only provides critical diagnostic information, but also the venting of cerebrospinal fluid (CSF) pressure usually provides significant decrease in the headache symptoms. The patient should be placed in the lateral decubitus position for the lumbar puncture. Once the needle is placed in the appropriate location following penetration of the dura, the patient is asked to relax their breathing and stretch their legs slightly, and then the manometer is attached for direct measurement of the pressure. Typically, CSF pressure is $<$180 mm of water. In pseudotumor the pressure will exceed 200 mm of water and may even flow over the

top of the manometer. CSF must be collected for glucose, protein, cell counts, and cultures. CSF cytopathology may be an option.

Idiopathic intracranial hypertension is the most frequently encountered entity in this category and can be caused by multiple disorders including endocrinopathies (hypothyroidism, Addison disease, oral steroids), pregnancy, drugs (tetracycline and oral contraceptives), vitamin A intoxication, anemia, systemic lupus erythematosis, chronic sinopulmonary infection, and obesity. Once the diagnosis is established, the carbonic anhydrase inhibitor, acetazolamide, can be used to lower CSF pressures. The side effects are few and include paresthesias, polyuria, and sedation. The dose is typically 250 mg twice a day up to 1000 mg per day. There is a once daily preparation available. The recovery is slow, over weeks or months. If obesity is a contributing factor, a weight loss program is recommended. If the visual symptoms are severe, progressive, or if there is visual compromise, ophthalmologic intervention may be necessary with performance of an optic nerve sheath fenestration.

Summary

Headaches are very common during childhood and become increasing more frequent during adolescence. Headache can be caused by *primary* entities such as migraine or tension-type, or the pain may result from *secondary* causes such as brain tumors, increased intracranial pressure, drug intoxications, paranasal sinus disease, or acute febrile illnesses.

The evaluation of the child with headache hinges on a thorough medical history exploring the clinical features, associated symptoms, and temporal pattern of the headache syndrome. Physical and neurological examination, in most instances, provide reassurance as to the absence of serious underlying organic pathology such as brain tumor or idiopathic intracranial hypertension. The principle indication for performance of ancillary diagnostic testing rests on information or concerns revealed during this fundamental process.

The first step of management is to establish the appropriate diagnosis and to provide confident reassurance to the patient and their family as to what the headache is caused by (ie, migraine) and what it is not caused by (ie, brain tumor). This alone is our most important therapeutic intervention in most clinical situations.

The management options for the primary headache syndromes, principally migraine and tension-type headache, are based on the "headache burden," or the degree of disability imposed by the headache. The therapeutic options include biobehavioral modifications, acute, and/or preventative pharmacological agents. The pathway chosen for treatment must be individually tailored, flexible, available, and sensitive to comorbid conditions.

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