Pediatric Headache: A Review

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Educational Gap

Headaches are common in children; while most are caused by a benign problem or primary headache disorder, headaches can be a sign of a serious underlying condition. Pediatricians must be aware of the most recent recommendations for evaluating and managing headaches.

Objectives

After reading this article, readers should be able to:

1. **Understand the evaluation of a child who has headache.**
2. **Recognize the diagnostic criteria for pediatric migraine.**
3. **Recognize "red flags" for elevated intracranial pressure or other underlying conditions in the child who has headache.**
4. **Discuss treatment strategies for migraine, tension, and chronic headache disorders.**

Introduction

Headaches are common in children and adolescents and are a frequent chief complaint in office and emergency department visits. The vast majority of childhood headaches are due to a primary headache disorder, such as migraine, or an acute, relatively benign process, such as viral infection. However, clinicians also need to consider other causes of headaches in children. Even when headaches are benign, they may cause significant dysfunction for the child and family and must be managed appropriately to minimize disability and optimize function. In this review, we discuss the epidemiology of childhood headache, evaluation of the child who has headaches, when to consider secondary headache syndromes, and the diagnosis and management of primary headache disorders such as migraine and tension-type headaches.

Epidemiology of Childhood Headache

Acute and chronic headaches are relatively common in children and adolescents, although estimates of the precise prevalence of headache and migraine vary widely. Depending on the study definition of headache, population involved, and time periods studied, 17% to 90% of children report headaches, with an overall prevalence of 58% reporting some form of headache in the past year. (1)(2) Headaches are slightly more common in young boys than girls (age <7 years), but around the time of puberty, this ratio begins to change. Although the prevalence of headache increases with age in both genders, the prevalence of headache increases much more sharply in girls until it reaches adult levels in late adolescence, when the prevalence of headache is significantly higher in women than in men. In adolescence, 27% of girls and 20% of boys describe frequent or severe headaches, and 8% of girls and 5% of boys have had a migraine in the past year. (1)(3) In adults, over 80% of women and 60% of men have had a headache, and 15% of women and 6% of men report having had a migraine in the past year. (1)(2)(4)(5)

Abbreviations

CSF:	cerebrospinal fluid
ICH:	intracranial hemorrhage
ICP:	intracranial pressure
IIH:	idiopathic intracranial hypertension
NDPH:	new daily persistent headache
NSAID:	nonsteroidal anti-inflammatory drug
SVT:	sinus venous thrombosis
TAC:	trigeminal autonomic cephalalgia

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Childhood Headache Patterns

Although the majority of children who have headaches do not seek medical care, severe or recurrent acute headaches and chronic headaches are common causes of office and emergency department visits for families who are concerned about the cause of the child's headache (often worried about a brain tumor) and are looking for ways to prevent or manage the headaches. Although serious secondary causes of headache are not common, it is important to ensure that there is no significant underlying disorder that is causing the headaches.

Headaches can be divided into four basic patterns, the recognition of which facilitates the evaluation and diagnosis of the headache: 1) acute; 2) acute recurrent (or episodic); 3) chronic progressive; and 4) chronic nonprogressive (Fig). (6) A thorough history and examination are essential to classify and manage the headache appropriately. Acute recurrent and chronic nonprogressive headaches are most likely related to a primary headache disorder, although other secondary causes of headaches should be considered in the appropriate circumstances. Chronic progressive headaches are the most worrisome type of headache and deserve a thorough evaluation, most often including neuroimaging. A single acute headache is most often benign, usually triggered by an underlying primary headache disorder or viral infection; however, other serious disorders can cause acute severe headaches (Table 1). (7)

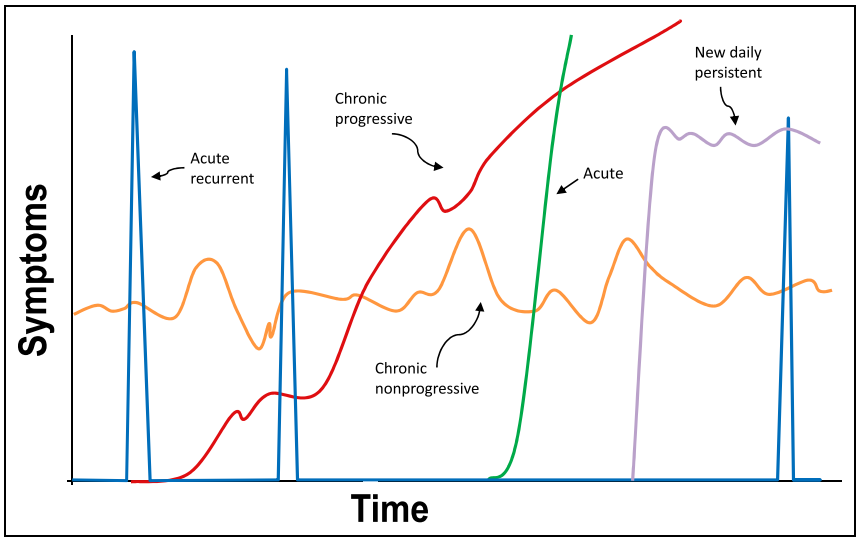

Figure. Headache patterns. (Adapted with permission from Rothner AD. The evaluation of headaches in children and adolescents. *Semin Pediatr Neurol*. 1995;2[2]:109–118.)

Primary Headache Syndromes

Migraine

Migraine is common in childhood, with a prevalence of 1% to 3% in children age 3 to 7 years and 8% to 23% in adolescence, (3) when migraine is much more common in girls than in boys. Migraine is also a common cause of acute headaches that lead to evaluation by a medical professional. The definition of migraine is outlined in Table 2; migraine typically is diagnosed via history and examinations without neuroimaging.

Migraine headaches without aura are more common than those with aura, but both can affect children. It may be difficult to diagnose migraine in very young children because symptoms of vomiting or vertigo may be more prominent than headache. Migraine headache pain may be unilateral or bilateral in children, often is frontal or temporal, and typically is a pounding or pulsing pain. Exclusively occipital pain is unusual and should raise suspicions for another disorder.

Migraine is a primary neurologic disorder. The pathophysiology of migraine is presumed to be the same in children and adults. It is believed that the mechanisms of migraine are based on complex interactions between the neural and vascular systems, including cortical spreading depression, abnormal neuronal excitability, serotonin activity, inflammatory response, and trigeminal neurovascular activation with signal transmission through the thalamus to the cortex. (8) Migraine is no longer believed to be a simple phenomenon of isolated vasoconstriction-triggering pain but a complex cascade of events. We know that mutations in a calcium channel gene (CACNA1A), a sodium/potassium pump (ATP1A2) gene, and a sodium channel (SCN1A) gene and mitochondrial dysfunction all can result in migraine. There are likely to be other genetic differences, yet to be revealed, that can alter neuronal or glial function and lead to the clinical syndrome of migraine. However, migraine is multifactorial; although migraine has a strong genetic component, the heritability pattern is not simple, the clinical manifestations can be different in various family members, and migraine has a very strong environmental component. Although migraines have been described for thousands of years and studied for over 50 years, the

Table 1. Causes of Pediatric Headache

- Acute headache
  - Migraine
  - Viral respiratory infection, streptococcal pharyngitis
  - Meningitis/encephalitis
  - Intracranial hemorrhage
  - Tumor
  - Toxic exposures: alcohol, toxins, illicit drugs, medications
  - Trauma
  - Stroke
  - Malignant hypertension
  - Vasculitis
- Episodic recurrent headaches
  - Tension-type headache
  - Migraine with or without aura
  - Fasting/eating disorders
  - Recurrent toxic exposures: alcohol, toxins, illicit drugs, medications
  - Recurrent sinus disease
  - Seizure-associated headache
  - Mitochondrial disease
  - Trigeminal autonomic cephalalgias
- Chronic progressive headaches
  - Elevated intracranial pressure
  - Tumor
  - Vascular malformations
  - Infection
  - Sinus venous thrombosis
  - Idiopathic intracranial hypertension
  - Endocrine disease: thyroid or parathyroid disease
  - Chiari malformation
  - Vasculitis
- Chronic nonprogressive headaches
  - Chronic tension-type headaches
  - Chronic or transformed migraine
  - New daily persistent headache
  - Chronic sinus disease
  - Dental disease
  - Sleep apnea
  - Idiopathic intracranial hypertension
  - Thyroid disease
  - Chiari malformation
  - Fasting/eating disorders
  - Chronic posttraumatic headache
  - Chronic trigeminal autonomic cephalalgias

exact pathophysiologic mechanisms of migraine remain unknown.

Migraine headaches in children typically are shorter than adult migraine attacks and may last only 30 to 60 minutes. Children often seek a quiet dark place to go during an attack due to phonophobia or photophobia. Anorexia, nausea, and vomiting also are common during a migraine attack. Sleep often relieves the headache.

Other symptoms that may be associated with a migraine attack include dizziness, blurry vision, difficulty reading, stomach pain, flushing, sweating, pallor, and dark circles around the eyes. Children may have difficulty describing the pain or associated symptoms; asking the child to draw his or her headache can help to define the headache. A family history of migraine or headaches is common, although the pattern of headaches may be different in other family members. Common triggers for a migraine attack include stress, "let-up" from stress, fatigue and poor sleep, illness, fasting, and dehydration. An obvious food trigger is not common but may be a factor for some children who experience migraine.

Migraine With Aura

Most children do not have aura with migraine, and many of those who do have aura sometimes have headaches without aura. Auras usually occur less than 30 minutes before the headache and last only 5 to 20 minutes. A typical visual aura may consist of scotomata, transient blurry vision, zig-zag lines, or scintillations, but more complex visual changes such as those seen in Alice in Wonderland syndrome (visual distortions that include sensation that objects are bigger or smaller than they are; objects appear to be moving when they are still; or objects have shattered like glass) can occur. Other types of aura also occur, including sensory changes (numbness or tingling), confusion, weakness, amnesia, or aphasia. These symptoms are notable, but the onset of symptoms in migraine typically occurs over a longer time period than the symptoms of stroke or seizure. The symptoms of aura are completely reversible, usually last <30 minutes, and often are recurrent over time. Patients who have neurologic symptoms that are prolonged, not related to headache, or not completely reversible should have an evaluation to rule out other underlying conditions.

Other Migraine Headache Syndromes

Less common subtypes of migraine include basilar, confusional, and hemiplegic. In basilar migraine, the aura is characterized by vertigo, ataxia, nystagmus, dysarthria, tinnitus/hyperacusis, bilateral paresthesias, diplopia, or visual disturbance. The aura can be unilateral or bilateral but does not involve motor weakness; the accompanying headache often is occipital.

Confusional migraine is characterized by altered mental status, often accompanied by aphasia or impaired speech and followed by a headache. This state can be triggered by relatively mild head trauma, and the initial

Table 2. Pediatric Migraine Criteria

Migraine without aura
- A. At least five attacks fulfilling criteria B–D
- B. Headache attacks lasting 1–72 hours (untreated or unsuccessfully treated)
- C. Headache has at least two of the following characteristics:
  1. Unilateral location, although may be bilateral or frontal (not exclusively occipital) in children
  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 headache at least one of the following:
  1. Nausea and/or vomiting
  2. Photophobia and phonophobia (which may be inferred from behavior)
- E. Not attributed to another disorder

Migraine with aura
- A. At least two attacks fulfilling criteria B–D
- B. Aura consisting of at least one of the following:
  1. Fully reversible visual symptoms including positive features (eg, flickering lights, spots, or lines) and/or negative features (ie, loss of vision)
  2. Fully reversible sensory symptoms including positive features (ie, pins and needles) and/or negative features (ie, numbness)
  3. Fully reversible dysphasic speech disturbance
- C. At least two of the following:
  1. Homonymous visual symptoms and/or unilateral sensory symptoms
  2. At least one aura symptom develops gradually over ≥5 min and/or different aura symptoms occur in succession over ≥5 min
  3. Each symptom lasts ≥5 and <60 min
- D. Headache fulfilling criteria B–D for migraine that begins during aura or follows aura within 60 minutes
- E. Not attributed to another disorder

Adapted with permission from Headache Classification Subcommittee of the International Headache Society. The International Classification of Headache Disorders: 2nd edition. *Cephalalgia*. 2004;24(suppl 1):9–160.

episode warrants a complete evaluation to rule out other disorders and intoxication. Hemiplegic migraine is a rare migraine variant that can be familial or sporadic and is characterized by prolonged hemiplegia, numbness, aphasia, and confusion. Genetic testing is available to identify mutations in three genes (CACN1A, ATP1A2, and SCN1A) that have been associated with familial hemiplegic migraine.

Tension Headache

Tension-type headache probably is the most common type of headache in childhood but generally is less disabling than migraine. In contrast to migraine, the pain is mild to moderate, may last for 1 hour or for several days, and often is described as "band-like," pressure, or tightening. Triggers may be similar to migraine and include stress, fatigue, and illness but also include muscle pain and tension, particularly in the neck and shoulders.

Tension headaches may be episodic (<15 days per month) or chronic (≥15 days per month). A thorough history to identify stressors, depression, or other factors associated with these headaches is important. Little is known about the pathophysiology of tension-type headaches. Some believe that nociceptive input from cranial/cervical myofascial components triggers these headaches initially, and if this noxious input is sustained, central sensitization can occur, so that an individual becomes more sensitive to these impulses and develops chronic headaches.

Chronic Headache

Chronic daily headache is defined as ≥15 headache days per month. There are three major categories of chronic daily headaches in children: chronic migraine, chronic tension-type headaches, and new daily persistent headache (NDPH).

Chronic or transformed migraine is not uncommon in adolescents. These children typically have a history of episodic migraine that becomes more and more frequent until they have more than 15 days per month of headache. Often they have few or no headache-free days. Typically, the serious migraine symptoms that were associated

initially with the headache, such as vomiting and severe head pain or aura, diminish somewhat as the headaches become more frequent, although patients still may have "spikes" of severe head pain at times.

Chronic tension-type headaches may share similarities with chronic migraines once the headaches become daily, and it can be difficult to classify daily headaches as tension or migraine. However, those who have tension-type headaches should not have a history of episodic migraine. Preventive treatment should be considered when the child is having 4 or more days of disabling headache per month. It is also critical to address lifestyle issues such as inadequate or irregular sleep, stress, inadequate or inappropriate food or caffeine intake, inadequate exercise, and poor hydration. Depression and anxiety are common issues for patients who have chronic headaches and may contribute to the headache.

NDPH is characterized by the occurrence of a new headache that becomes daily within 3 days of onset and is not caused by another disorder. Given the abrupt onset of this headache, children who have this type of headache should have an evaluation for secondary disorders. NDPH often is triggered by a viral illness but may be caused by mild head trauma or surgery, or a trigger may be absent.

Other Primary Headache Syndromes

Trigeminal autonomic cephalalgias (TACs) are rare in children. The treatments for migraine or tension headaches may not be effective for TACs, and recognition of these headaches is therefore important. This diagnostic group includes cluster headaches, paroxysmal hemicranias, and SUNCT (short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing). These paroxysmal headaches typically are accompanied by autonomic symptoms, such as ipsilateral eye redness, tearing, nasal congestion, rhinorrhea, eyelid swelling, forehead or facial sweating, miosis, or ptosis. Another rare headache that is important to recognize is primary stabbing headache. These patients have stabbing pain in the first division of the trigeminal nerve (orbit, temple, and parietal area) that lasts for a few seconds and recurs in an irregular pattern. Given that secondary causes of TACs and stabbing headaches have been reported, children who have these symptoms should undergo neuroimaging, although most will have normal scan results.

Secondary Headaches

Abnormal Intracranial Pressure

Elevated intracranial pressure (ICP) is an uncommon but important cause of pediatric headaches and has various causes. Hydrocephalus may result from a space-occupying lesion, blockage of cerebrospinal fluid (CSF) flow via aqueductal stenosis, or impaired CSF absorption. Increasing the volume of tissue or fluids in the cranial vault (eg, mass lesions, edema, inflammation, hemorrhage) also can lead to a dramatic increase in ICP.

Headaches are the most common presenting symptom of elevated ICP. Typically, these headaches are progressive, may cause nighttime wakening, and are worse with the Valsalva maneuver or exertion. Children who have elevated ICP often experience persistent vomiting, neurologic deficits, lethargy, or personality change. Other signs of elevated ICP include papilledema and palsies of the third, fourth, or sixth cranial nerves, resulting in eye movement or pupillary abnormalities.

Low ICP also can cause headaches. Intracranial hypotension should be considered if there is a risk for CSF leak (eg, spinal surgery, trauma, connective tissue disease). Meningeal enhancement on brain magnetic resonance imaging may be seen with intracranial hypotension.

Idiopathic Intracranial Hypertension

Idiopathic intracranial hypertension (IIH), sometimes called pseudotumor cerebri, is elevated ICP without evidence of a specific cause. Daily headache is the most common symptom of IIH and may be associated with nausea and vomiting and other migrainous features, but the headache often is poorly characterized. Classic symptoms of IIH include transient obscuration of vision, tinnitus, and diplopia due to cranial nerve dysfunction. In young children, the most common complaints are headache, stiff neck, strabismus, irritability, apathy, somnolence, dizziness, and ataxia.

Children are more likely to have an underlying condition associated with IIH than adults (Table 3); a thorough evaluation in addition to accurate assessment of opening pressure is thus essential when IIH is suspected in a child. The patterns of IIH in adolescence are similar to adult patterns; more female patients than male patients are affected, and obesity is associated with IIH. However, in younger children, when IIH is less common, the genders are affected equally, and obesity is not strongly associated with IIH.

Infection

Acute viral illness with fever is the most common cause of pediatric headache evaluated in the emergency department. (9) Typically, these children will have an acute onset of headache, and the headache resolves as the other viral symptoms dissipate. Many other systemic infections can be associated with headache, including streptococcal pharyngitis, sepsis, Lyme disease, *Bartonella* infection,

Table 3. Conditions Associated With Intracranial Hypertension

- Cerebral venous sinus thrombosis
- Medications
  - Thyroid replacement
  - Corticosteroids (particularly withdrawal)
  - Growth hormone
  - Levothyroxine
  - Cytarabine, cyclosporine
  - Lithium
  - Levonorgestrel
  - Sulfa antimicrobials
  - Tetracycline antibiotics (minocycline, doxycycline)
  - Vitamin A
  - Cis-retinoic acid
- Lyme disease
- Anemia
- Antiphospholipid antibody syndrome
- Occult craniosynostosis
- Sarcoidosis
- Sleep apnea
- Systemic lupus erythematosus

rickettsial diseases, and human immunodeficiency virus infection, but headache rarely is the only symptom. Viral infection, particularly with Epstein-Barr virus, can be associated with the onset of NDPH.

Although sinusitis may cause or trigger headaches in some children, the majority of patients diagnosed as having "sinus headaches" have some form of primary headache syndrome. Sinus-related pain generally is pressure-like and dull periorbital pain, worse in the morning, associated with nasal congestion, and lasts for days at a time. It is not associated with nausea, visual changes, phonophobia, or photophobia.

Meningitis or encephalitis are the causes of acute headaches in 2% to 9% of children evaluated for headache in the emergency department. (9) Headaches due to meningitis or encephalitis often are associated with photophobia, nausea, vomiting, and pain with eye movements. These patients typically also have symptoms such as fever, altered mental status, and nuchal rigidity, although fungal meningitis may be more indolent.

Structural Disorders

Although families and patients worry that a brain tumor is causing the headaches, tumors are uncommon causes of headache in children. Tumors and other space-occupying lesions, such as large arachnoid cysts or vascular malformations, can cause headache via hydrocephalus, mass effect, or hemorrhage. One should consider a space-occupying lesion if the child has "red flag" symptoms noted in the following discussion (Table 4) or if the child has a history of exposure to ionizing radiation or a syndrome (such as tuberous sclerosis or neurofibromatosis) that is associated with tumors.

Chiari I malformation, characterized by the herniation of the cerebellar tonsils >5 mm below the foramen magnum, may cause headache. The classic symptoms include occipital headaches, cough headaches or syncope, sensory disturbance, weakness, ataxia, vertigo, or other cranial nerve dysfunction. Confirming that headaches are due to a Chiari malformation can be challenging because more than 30% of patients with Chiari I malformation on magnetic resonance imaging are asymptomatic, radiologic findings often do not correlate with clinical symptoms, and other causes of headache not related to Chiari malformations are common.

Vascular Disorders

Spontaneous intracranial hemorrhage (ICH) and ischemic stroke are rare causes of headache in children. Although an acute "thunderclap" headache is the classic presenting symptom of ICH, most children who have ICH or ischemic stroke have additional signs or symptoms by the time they present to medical care. ICH should be considered in patients who have an acute onset of severe headache, particularly if the patient has an

Table 4. Red Flags for Secondary Headache

- Progressive pattern of the headache: becoming more severe and/or more frequent
- Increased headache with straining, coughing, or sneezing
- Explosive or sudden onset of severe headache (<6 mo duration)
- Systemic symptoms: fever, weight loss, rash, and joint pain
- Secondary risk factors: immunosuppression, hypercoagulable state, neurocutaneous disorder, cancer, genetic disorder, and rheumatologic disorder
- Neurologic symptoms or signs: altered mental status, papilledema, abnormal eye movements, or other abnormalities or asymmetries on neurologic examination
- New or different severe headache, change in attack frequency, severity, or clinical features
- Sleep-related headache, headache waking the patient from sleep, or headache always present in the morning

abnormal result on neurologic examination or a disorder that places him or her at risk for hemorrhage.

In ischemic stroke, neurologic symptoms come on abruptly and persist, typically do not progress from one side of the body to the other, and typically are not recurrent. In contrast, the symptoms of migraine aura usually last less than 30 minutes, may involve both sides of the body or progress from one side of the body to the other, and often are recurrent over months to years.

Sinus venous thrombosis (SVT) is another uncommon cause of secondary headaches in children. The most common presenting symptoms of SVT in children are headache, focal neurologic signs, seizures, decreased level of consciousness, and papilledema. The vast majority have some risk factor for SVT, including head or neck infection, chronic systemic disease, or other prothrombotic state. Thus, SVT should be considered in patients who have headaches and other neurologic symptoms, particularly in those who have underlying conditions that place them at risk for thrombosis.

Trauma

Children who have severe or progressive headache or altered mental status after head injury should be evaluated emergently. Headaches after a head injury may be due to traumatic ICH or fracture but more commonly are due to posttraumatic headache *without* significant structural injury. One study concluded that children older than age 2 years who have normal mental status, no signs of skull fracture, no loss of consciousness, no vomiting, nonsevere mechanism of injury, and nonsevere headache do not need a computed tomography scan after head trauma. (10)

Posttraumatic headaches develop within 1 week of head trauma, concussion, or whiplash. These headaches may have qualities of migraine or tension headaches and often are associated with other postconcussive symptoms, including sleep disturbance, balance abnormalities, cognitive changes, and mood changes. The vast majority of posttraumatic headaches resolve within 2 weeks.

Children and teenagers who have posttraumatic headache (indeed, all who have sustained a concussion) should not return to sports or vigorous exercise until they are symptom-free at rest and while active and have been cleared by a trained medical provider. Once symptom-free, they should return to their regular activities in a step-wise fashion, as outlined in the 2009 Zurich Consensus Statement on Concussion in Sport. (11) Adolescents who have chronic posttraumatic headaches may benefit from returning to low-level "subthreshold" exercise (aerobic exercise that does not trigger worsening of symptoms), with supervision by a trained medical provider. (12)

Substances That Can Cause Headache

There are many substances that can cause headaches, including overuse or withdrawal of caffeine, alcohol use, illicit drug use, carbon monoxide poisoning, and lead toxicity. Medications also can trigger headaches due to the medication's primary mechanism of action, an idiosyncratic response to the medication, or medication withdrawal. Overuse of medications to treat headaches, especially analgesics, caffeine, opioids, ergotamines, and 5-hydroxytryptamine 1 (5-HT_1) receptor agonists (ie, the triptans), is associated with transformation from episodic to chronic headaches. Some medications that have been associated with headache are listed in Table 5. (13)

Systemic Disease and Headache

Metabolic Derangements and Endocrine Disorders

Fasting is a relatively common cause of headaches in children. Eating disorders also can trigger headaches but may be concealed by the patient. Hypothyroidism can cause headache and should be considered when evaluating for refractory headaches. Hypercapnia and

Table 5. Medications Associated With Headaches

Angiotensin-converting enzyme inhibitors
α- and β-adrenergic agonists and blockers
Amphetamines
Antiarrhythmics
Calcium channel blockers
Methylxanthines
Nitrates
Phosphodiesterase inhibitors
Sympathomimetics
Caffeine
Ergotamine
Estrogen
Opioids
Acid blockers: including famotidine and ranitidine
Antimicrobials: amoxicillin, metronidazole, sulfamethoxazole, trimethoprim, ciprofloxacin, gentamicin, nitrofurantoin, ofloxacin, tetracyclines
Immunoglobulin
Amiodarone
Corticosteroids
Oral contraceptives
Thyroid hormone replacement
Vitamin A and retinoic acid

Adapted with permission from Ferrari A, Spaccapelo L, Gallesi D, Sternieri E. Focus on headache as an adverse reaction to drugs. *J Headache Pain.* 2009;10(4):235–239.

hypoxia occur together in sleep apnea or hypopnea due to neuromuscular disease and are associated with headache. A sleep study may be indicated in a patient who has morning headaches and symptoms suggestive of sleep apnea.

Epilepsy

Peri-ictal headaches are common in children who have epilepsy. Typically, the association between the headache and seizure will be obvious. However, some seizures are characterized by episodes of altered mental status or visual disturbances followed by headache, which may be confused with migraine. The visual hallucinations in epilepsy typically are colored and rounded objects, rather than the jagged or scintillating impressions seen in migraine aura.

Mitochondrial Disease

Headache and migraine are frequent findings in mitochondrial disease. However, children who have significant mitochondrial disease typically also have problems with other organ systems and additional neurologic symptoms.

Dental Disease

Temporomandibular disorders have been associated with migraine, tension-type headache, and chronic daily headache. Malocclusion of the jaw and other dental problems also can cause headache.

Sickle Cell Disease

Children who have sickle cell disease are at risk for multiple serious causes of headache, including ischemic stroke, intracerebral hemorrhage, thrombosis, and chronic anemia. However, they also may have migraine or tension headaches, and young children who have sickle cell disease are more likely to have idiopathic headaches than age-matched controls. (14)

Hypertension

Acute, severe headaches may be the initial sign of a hypertensive crisis. However, mild to moderate hypertension typically does not cause significant headaches.

Rheumatologic Disease

Children who have rheumatologic disease often have headache. The causes of headache in rheumatologic disease can include aseptic meningitis, intracranial hypertension, SVT, vasculitis, intracerebral hemorrhage, ischemia, or headache without underlying pathology. Immunosuppressive agents and nonsteroidal anti-inflammatory drugs (NSAIDs) used to treat rheumatologic disorders also can cause headaches. Thus, children who have diagnosed or suspected rheumatologic disease and headache should have a thorough evaluation for secondary causes of headache.

Psychiatric Disease

Although depression and anxiety disorders are common in patients who have headaches, psychiatric disease usually is an exacerbating rather than a causative factor. Screening for depression or anxiety is beneficial because successful treatment of the headache will be difficult if psychiatric issues remain unaddressed. Headaches should be attributed to somatization disorder, psychotic disorder, major depressive disorder, or anxiety if those symptoms are prominent and if the headaches remit with treatment of the psychiatric disorder.

Evaluation of Headache in Children

History

The patient's history is the single most important factor in the evaluation of headache. Both the patient and the parents should be included in this discussion to gather a complete picture of the patient and his or her symptoms. The history should include characterization of the headache:

- How many different types of headache does the child have?
- When did the headaches begin? Was anything associated with headache onset?
- Are the headaches getting worse, staying the same, or improving? Are they getting more or less frequent? Are they more or less intense?
- Are there any triggers for the headaches?
- What are the headaches like? Where is the pain located? What does the pain feel like?
- Does the headache wake the child from sleep?
- Are there any headache patterns or triggers?
- Are there any other symptoms associated with the headache, or warning signs that a headache is coming (aura)?
- What does the child do during a headache?
- How long does the headache last?
- What makes the headache better or worse? (6)

Adapted from Rothner AD. The evaluation of headaches in children and adolescents. *Semin Pediatr Neurol.* 1995;2(2):109–118.

It is important also to obtain a detailed medical history because headaches may be associated with systemic illnesses and medications. For example, one would have a higher suspicion for secondary headache in a patient who has neurofibromatosis who is at risk for central

nervous system tumors, or in a patient who started minocycline just before headache onset and is at risk for intracranial hypertension. Review of other symptoms related or seemingly unrelated to headache is important because they may suggest systemic disease as a secondary cause of the headache (eg, a malar rash suggestive of systemic lupus erythematosus, cold intolerance and skin changes suggestive of hypothyroidism, a history of episodic torticollis or vertigo as a young child consistent with migraine precursors).

FAMILY HISTORY. Information regarding any family history of headaches, pain, and other medical disorders is important because migraine has a strong genetic component and other disorders related to headache may also run in the family. It is important to ask about family history of *any* type of headaches because other forms may be mentioned by the family when "migraine" is denied. It is helpful to get information about headaches in grandparents, siblings, aunts, and uncles because migraines may skip the parent (often the father) and manifest in the child (often the daughter), and the headache pattern often is different in different family members.

SOCIAL HISTORY. Discussion of social history also is critical because stressors at home, at school, or with friends can trigger or exacerbate headaches. A private conversation with an adolescent often is helpful because the teenager may not wish to discuss some issues in a parent's presence. This dialogue might include questions about conflict with friends or family, sexual activity, pregnancy, drugs, cutting behavior, physical or sexual abuse, bullying, depression, family finances, alcohol use, or eating disorders, all of which may affect headache.

Lifestyle Factors

Lifestyle factors often affect a headache pattern; it is therefore important to ask about sleep, diet, exercise, caffeine intake, and other activities. A headache diary can help to identify headache triggers or patterns. Inadequate sleep, poor hydration, and poor food choices are common, particularly in teenagers, and these factors often exacerbate or trigger headaches. Children and teenagers who have chronic headaches frequently do not get enough exercise, and regular appropriate exercise is an essential part of a headache management plan (Table 6). Caffeine intake more than 2 to 3 days per week may be a cause of rebound or medication overuse headaches. Clinicians should be aware of the presence of caffeine in soda and energy drinks.

Physical Examination

The evaluation should include measurement of heart rate, blood pressure, weight, and height in the context of a thorough physical examination looking for signs of systemic disease or focal findings that could be related to headaches. This procedure should include palpation of the face, neck, and shoulders, looking for nuchal rigidity, muscular or bony tenderness, trigger points, or allodynia (abnormal pain sensation with light touch, often associated with migraine); skin examination looking for signs of systemic disease, cutting behavior, or neurocutaneous syndromes; and oral evaluation looking for signs of dental disease.

A thorough neurological examination is essential to look for abnormalities in mental status, vision, eye movements, speech, sensation, strength, reflexes, gait, or coordination, particularly noting any focal abnormalities, significant asymmetries, or cranial nerve palsies. Funduscopic examination looking for evidence of papilledema, optic atrophy, or other abnormalities must be included in the examination.

"Red Flags" and Neuroimaging

Several risk factors are associated with an intracranial space–occupying lesion in children who have headache, including sleep-related headache, absence of family history of migraine, headache <6 months' duration, confusion, abnormal neurologic findings, lack of visual aura symptoms, and vomiting. Children who have more risk factors have a higher risk of having a brain lesion requiring surgery. (15) Other worrisome symptoms include headache associated with cough, urination, or defecation; recurrent and focal headache; exclusively occipital headache; change in headache type; and progressive increase in headache frequency or severity. Table 4 lists factors associated with serious secondary headache.

Table 6. SMART Headache Management

Sleep	Regular and sufficient sleep
Meals	Regular and sufficient meals, including breakfast and good hydration
Activity	Regular (but not excessive) aerobic exercise
Relaxation	Relaxation, stress reduction, and management
Trigger avoidance	Avoid triggers such as stress, sleep deprivation, or other identified triggers

One should consider neuroimaging to rule out a structural intracranial lesion if the child has symptoms noted here. Although there are no guidelines regarding the risks of serious secondary causes of headaches in very young children (less than age 3-5), because of the possibility of secondary headaches, neuroimaging should be considered thoughtfully in these young children who have significant recurrent headaches.

Brain magnetic resonance imaging is the modality of choice to investigate potential structural abnormalities, infection, inflammation, and ischemia; however, computed tomography scan is preferred if there is a concern for hemorrhage or fracture.

The American Academy of Neurology practice parameter regarding the role of neuroimaging in the evaluation of children who have recurrent headaches states:

1. Obtaining a neuroimaging study on a routine basis is not indicated in children who have recurrent headaches and normal results on neurologic examination.
2. Neuroimaging should be considered in children who have abnormal results on neurologic examination, the coexistence of seizures, or both.
3. Neuroimaging should be considered in children in whom there are historical features to suggest the recent onset of severe headache, change in the type of headache, or if there are associated features that suggest neurologic dysfunction. (16)

Other Testing

Further testing for children who have headaches should be considered if there is clinical suspicion of an underlying disorder such as meningitis, thyroid disease, or other systemic disease. If there is a suspicion for elevated ICP and the neuroimaging results are normal, lumbar puncture with measurement of opening pressure and measurement of CSF indices is appropriate.

Management of Primary Headache Syndromes

Once a diagnosis of migraine or tension headache has been established and serious secondary causes of headache have been excluded, headache education and management can begin. Education of the patient and family about primary headaches, reassurance that there is no serious underlying disorder, and unification of the patient, family, and provider on a treatment strategy and goal are essential. Successful management of the headaches will be difficult if this foundation is not in place. It is helpful for the patient to keep a headache diary to identify headache patterns and triggers and to evaluate treatment response. The four major domains of headache treatment include: 1) lifestyle modification; 2) acute headache management; 3) complementary treatments; and 4) preventive treatment. Many children will require only recognition and modification of headache triggers and instruction about appropriate acute headache management, but those who have chronic headaches often require a multifaceted treatment plan.

Lifestyle Changes and Stressors

Any lifestyle factors that could be triggering or exacerbating headaches must be addressed and modified if possible. This modification might include getting adequate

Table 7. Acute Treatment for Childhood Migraine

Drug	Dose
Acetaminophen	10–12.5 mg/kg q 4–6 h Adult: 650–1,000 mg q 6 h Maximum: <4,000 mg/d
Ibuprofen	10 mg/kg q 4–6 h prn Adult: 400–800 mg q 6 h Maximum: 3,000 mg/d
Naproxen sodium	5–7 mg/kg q 8–12 h prn Adult: 250–500 mg q 8 h Maximum: 1,250 mg/d
5-HT_1 agonists, triptans	
Rizatriptan[a]	Adult: 5–10 mg may repeat once in 2 h ODT or tablets Maximum: 15 mg/d
Zolmitriptan[b]	Oral (tablet or ODT) or nasal Adult 2.5–5 mg per dose; may repeat once in 2 h Maximum: 10 mg/d
Sumatriptan[b]	Oral: 25–100 mg, maximum 200 mg/d Nasal: • 4–6 y: 5 mg • 7–11 y: 10 mg • >12 y: 20 mg[c] • Adult maximum: 40 mg/d SC: 0.06 mg/kg, >12 y: 6 mg SC, Adult maximum: 12 mg/d SC
Almotriptan[d]	6.25–12.5 mg; may repeat dose once in 2 h Maximum: 25 mg/d

Maximum=maximum dose; ODT=oral disintegrating tablet; prn=as needed; qXh=every X hours; SC=subcutaneous.
[a]Approved for treatment of migraine in children 6- to 17-years-old.
[b]Not approved for pediatric use.
[c]Strong supporting efficacy and safety data in adolescents.
[d]Approved for use in children age 12 to 17 years.

and regular sleep and removing electronics from the bedroom at night; eating regular and nutritious meals (including breakfast); limiting caffeine intake to no more than 2 to 3 servings per week; maintaining adequate fluid intake; avoiding or managing stressors; and performing regular aerobic exercise (Table 6). For those with anxiety, depression, or significant stressors, management also should include consultation with a mental health provider to help manage these symptoms because these issues *must* be addressed in conjunction with treating the headaches. Without simultaneous management of depression, anxiety, or stressors, reasonable headache control is likely to be extremely difficult.

Acute Treatments

The most important factor in the acute treatment of migraine or tension headache is early intervention for a significant headache because early treatment is most likely to be effective. However, patients should not use acute treatments more than 2 to 3 days per week (<15 days per month for NSAIDs and <10 days per month for triptans or caffeine) to avoid developing medication overuse headaches.

In children, over-the-counter medications such as ibuprofen, naproxen, and acetaminophen often are effective for the management of migraine (Table 7). The correct dose for the child's weight should be reviewed with the parent because underdosing may result in treatment failure and overdosing can be harmful.

For more severe headaches, a dose of an NSAID can be combined with caffeine (such as a limited amount of soda, tea, or coffee) less than 9 days per month, as long the child is not consuming caffeine on a regular basis. If the child does use caffeine regularly, it should be withdrawn carefully, because caffeine withdrawal can cause rebound headaches.

If NSAIDs are not effective, one may consider using triptans in appropriate circumstances. Although many different triptans are available for use in adults, only rizatriptan has been approved for migraine treatment in children age 6-17 and almotriptan has been approved for use in adolescents. This situation is due primarily to difficulty in study design (ie, overcoming the high placebo response in children) rather than current safety concerns.

There are data to support the use of sumatriptan (subcutaneous and nasal) and rizatriptan in children age >6 years, and zolmitriptan (oral and nasal) in children age >12 years (Table 7). (17) Opiates and barbiturates are not indicated for the treatment of primary pediatric headache disorders. Opiates may alter the pain response, increasing the risk of chronification of pain, and both compounds can lead to overuse headaches and addiction.

Antinausea medications can be useful adjuncts to the NSAIDs and triptans when patients have significant nausea and vomiting with their migraines. Prochlorperazine and metoclopramide are effective in the acute emergency department setting and may also be helpful in the outpatient setting. Although these medications do post a risk of dystonic reaction, these dopamine antagonists may help treat the underlying migraine as well as the nausea and vomiting. Ondansetron also has been used as an antiemetic in migraine and has a lower risk of adverse effects than some other antiemetic agents, although it is also more expensive (Table 8).

Complementary Medicine

Complementary therapies can be very helpful in the management of chronic or recurrent episodic headache. Biobehavioral techniques that may be successful include biofeedback therapy, relaxation techniques, hypnosis, acupuncture, and training in the use of coping mechanisms. Appropriate physical therapy or massage therapy also can be very helpful in some circumstances, particularly if the child has muscle pain or tension.

Preventive Therapy

Most headache specialists agree that daily therapy designed to prevent migraines should be considered when a patient experiences ≥4 days of disabling headaches per month. Many families prefer to try supplements or "nutraceuticals" before using prescription medications.

Table 8. Antiemetic Agents for Pediatric Migraine

Drug	Dose	Toxicity
Promethazine	0.25–0.5 mg/kg/dose Adult:12.5–25 mg/dose	Sedation Dystonic reactions[a]
Prochlorperazine	2.5–5 mg bid prn Adult: 5–10 mg q 6–8 h prn Maximum daily dose: 40 mg/d po Adult rectal dose: 25 mg	Sedation Dystonic reactions
Ondansetron	4–8 mg q 8 h • <15 kg: 0.2 mg/kg • 15–30 kg: 4 mg • >30 kg: 4–8 mg	Sedation Dystonic Reactions

prn=as needed; po=oral; q 8 h=every 8 h.
[a]Oculogyric crisis (managed with intravenous diphenhydramine).

These options may be as effective as some prescription medications and generally have fewer adverse effects. There is also a high placebo response rate in children who have headaches. Before beginning any preventive therapy, it is important to discuss expectations with the family because any preventive therapy typically takes at least 8 to 12 weeks to cause a recognizable effect. Switching preventive treatments every few weeks due to presumed ineffectiveness without an adequate trial will be unproductive and frustrating for all involved. A headache diary will help to assess the efficacy of the treatment over several months.

Supplements/Nutraceuticals

Although there are few randomized controlled trials of supplements for the management of headaches in

Table 9. Selected Preventive Medications for Pediatric Migraine

Drug	Dose	Toxicity
Cyproheptadine	0.25–1.5 mg/kg per day Adult: 4 20 mg/d tid	Sedation, dry mouth Weight gain
Tricyclic antidepressants		
Amitriptyline	10–50 mg qhs 0.1–1 mg/kg per day Maximum: 50–100 mg for headache	Sedation Weight gain May exacerbate cardiac conduction defects (consider baseline electrocardiogram)
Nortriptyline	10–75 mg qhs	Suicidal thinking, mood changes
Antiepileptics		
Topiramate	1–2 mg/kg per day for headache Typical adult dose: 50 mg bid Maximum: 800 mg bid for seizures	Sedation, paresthesias, appetite suppression/weight loss, glaucoma, kidney stones cognitive changes, word finding difficulty, mood changes, depression
Valproic acid	20–40 mg/kg per day; adult: 500–1,000 mg/d	Weight gain, bruising, hair loss, hepatotoxicity, ovarian cysts, teratogenic, thrombocytopenia, leukopenia, mood changes, depression
Gabapentin	10–40 mg/kg per day Adult: 1,800–2,400 mg/d Maximum: 3,600 mg/d	Fatigue, ataxia, tinnitus, gastrointestinal complaints, mood changes, depression
Antihypertensives		
Propranolol[a]	2–4 mg/kg per day Adult: 160–240 mg/d	Hypotension Sleep disorder Decreased stamina Depression
Verapamil	4–10 mg/kg per day divided tid <12 y: ≤120 mg 13–18 y: 240 mg	Hypotension, nausea, atrioventricular block Weight gain
Selected supplements used for headache prevention		
Riboflavin/vitamin B_2	50–400 mg	Yellow urine (25 mg may be effective; studies done using 400 mg/d)
Melatonin	1–6 mg before bed	Vivid or disturbing dreams
Magnesium oxide	9 mg/kg per day tid	Diarrhea Modify dose with renal dysfunction
Coenzyme Q10	100 mg/d	Rash, irritability Gastrointestinal symptoms
Migralief or Children's Migralief (B_2/magnesium/feverfew)	1 capsule 1–2 times/d	Yellow urine, diarrhea

bid=twice a day; Maximum=maximum dose; qhs=at bedtime; tid=3 times a day.
[a]Avoid when patient has asthma or diabetes; use caution when patient has depression.
Adapted from Lewis DW. Headaches in children and adolescents. *Curr Probl Pediatr Adolesc Health Care*. 2007;37(6):207–246.

children, there are several options that may be effective and are unlikely to cause harm. Riboflavin (vitamin B_2) seems to be effective for the treatment of adult migraine, using doses from 25 to 400 mg per day. (18)(19) Magnesium also has been used for the management of migraine. One pediatric study found that children who took magnesium oxide had a significant decrease in headache frequency over time, whereas those given placebo did not. (20) However, the most useful form of magnesium is not clear; other forms of magnesium may be more bioavailable or less likely to cause diarrhea than magnesium oxide, but these forms have not been studied in migraine. The typical adolescent dose of elemental magnesium is 350 to 500 mg per day (Table 9).

Coenzyme Q10 also may be helpful for the management of migraine and has few troublesome adverse effects. Butterbur extract (*Petasites hybridus*) also has been used for the management of migraine, but this plant naturally contains alkaloids that can be hepatotoxic or carcinogenic if not processed correctly; using a reputable source that is "PA free" is thus essential. There are reports of the use of melatonin to treat chronic daily headaches in teenagers and help manage sleep disruption; melatonin may therefore be particularly beneficial for teenagers with headache who have insomnia (Table 9).

Prescription Preventive Medications

There are many options for preventive therapy for migraine, but relatively few have been studied in rigorous, randomized controlled studies in children. In 2004, the American Academy of Neurology practice parameter concluded that flunarizine (a calcium channel blocker not available in the United States) is probably effective, but that there were conflicting or insufficient data to make recommendations for the use of other medications for the management of pediatric migraine. (21)

Since then, several studies have found that topiramate is significantly more effective than placebo for the management of pediatric migraine. (22)(23)(24) Other medications that are used typically for the prevention of pediatric migraine include β-blockers such as propranolol and tricyclic antidepressants such as amitriptyline and nortriptyline. Valproic acid also is used to treat migraines; however, this agent is teratogenic and may have other toxic effects and is therefore not the best first-line treatment for teenage girls. A nightly dose of cyproheptadine may be particularly useful in younger children or those who have environmental allergies and migraine. Other medications that have been used for migraine headache prevention include gabapentin and verapamil (Table 9). (25)

Prescription preventive medications should be started at a low dose and gradually increased to the goal or effective dose to minimize the risk of adverse effects. The choice of prescription preventive headache medication often is based on comorbid factors. For example, amitriptyline may be a reasonable choice for a teenager who is active and has difficulty sleeping at night but would not be a good choice for a child who is sleeping well and fatigued; topiramate may be a good option for an overweight adolescent but would not be a good choice for a thin 12-year-old who has a family history of kidney stones; and propranolol and low-impact aerobic exercise may be a good option for a child who has symptoms of postural orthostatic tachycardia syndrome but is not a good choice for an asthmatic child or competitive athlete.

Treatment of Unusual Headache Syndromes

There are few studies of the therapy of NDPH, but treatment strategies include typical migraine preventive medications (eg, topiramate, tricyclic antidepressant agents) and complementary therapies such as biofeedback, psychotherapy, physical therapy, massage, and education regarding coping skills. Some have suggested using acne doses of minocycline or doxycycline due to an elevation in the CSF of tumor necrosis factor-α found in a study of adults who have NDPH. These medications may lower levels of this cytokine in CSF. (26) Some TACs are responsive to indomethacin. Primary stabbing headaches often respond to indomethacin.

Summary

- Although most pediatric headaches are due to benign illness or a primary headache syndrome, clinicians must be able to recognize disorders that can cause secondary headache. Failure to identify and treat the underlying cause of a child's headache, whether it is due to migraine, viral illness, or serious systemic disease, can lead to morbidity and prolonged suffering.
- The most important factors in the evaluation and management of a child who has headaches are:

1. A comprehensive history detailing headache characteristics and any disorders, symptoms, or exposures that may be associated with the headache. Social and family history is important.
2. A complete physical and neurologic examination with attention to signs or symptoms that could be associated with a secondary cause of headache.
3. Further testing if indicated by the history and examination findings.
4. Creation of a multifaceted treatment plan with the child and family that is appropriate for the patient's

headache and is endorsed by the patient, family, and medical provider.

Use of these techniques in combination with a good understanding of primary and secondary headache syndromes will help to provide optimal care for children who have headaches.

- Headaches are common in childhood. Obtaining a neuroimaging study on a routine basis is not indicated in children who have recurrent headaches and normal results on neurologic examination (American Academy of Neurology 2002 Practice Parameter).
- Secondary causes of headache should be considered in children who have abnormal neurologic findings, who have had recent onset of severe headache, or who experience a new severe headache and in those with systemic disease or medication use that increases the risk of abnormal intracranial pressure, hemorrhage, thrombosis, intracranial infection, or structural lesion (according to the American Academy of Neurology 2002 Practice Parameter and strong research evidence).
- Treatment of primary episodic headaches, such as migraine or tension-type headache, should include assessment and modification of problematic lifestyle factors and stressors and appropriate acute headache treatment. Chronic or recurrent headache treatment may also include complementary therapies or preventive daily medications (according to expert opinion and some research evidence).

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1. A 4-year-old boy comes in with a complaint of headache. His father asks whether a "brain scan" should be performed. Which of the following characteristics would be the strongest indication for a magnetic resonance imaging study of this child's brain?
   A. Age under 5 years.
   B. Detection of a slight limp on examination.
   C. Headache that awakens him from sleep.
   D. Male gender.
   E. Unilateral headache.
2. A 12-year-old girl presents to your office with a history of frequent headaches that sometimes make her miss school. You are trying to differentiate between migraine and tension headache. Which of the following statements is true and will help you to differentiate?
   A. Migraine headaches are more likely to affect boys.
   B. Migraine headaches are relieved by exercise.
   C. Migraine headaches cause a "band-like pressure" on the head.
   D. Migraine headaches typically last for several hours.
   E. Migraine pain is throbbing and severe.
3. A 15-year-old girl who has just started to take acne medication presents to your office with poorly localizing daily headaches, blurry vision, and tinnitus. Of the following, which diagnosis is most likely to explain the findings above?
   A. Idiopathic intracranial hypertension.
   B. Medulloblastoma.
   C. Migraine headache.
   D. Tension headache.
   E. Trigeminal autonomic cephalalagia (cluster headache).
4. You are counseling a parent of a 17-year-old boy who has frequent tension headaches. The family and young man would prefer to try lifestyle interventions before proceeding to medications. Which of the following lifestyle interventions might be helpful in promoting headache reduction?
   A. Coffee or tea with breakfast daily.
   B. Limiting fluid intake to 40 ounces daily.
   C. Regular aerobic exercise.
   D. Skipping breakfast during weekends to allow for extra sleep.
   E. Television watching before sleep.
5. A 14-year-old girl has been diagnosed as having migraine. The headaches occur twice weekly and have caused her to miss school at least once per month. The family is interested in a prophylactic medication to prevent her attacks, and you plan to start amitriptyline. Of the following studies, which is indicated as part of amitriptyline therapy?
   A. Chest radiograph.
   B. Complete blood count.
   C. Electrocardiogram.
   D. Serum alanine aminotransferase.
   E. Serum creatinine.

Pediatric Headache: A Review

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