Chapter 165: Headache

Michael Harrigan; Ana C. G. Felix

INTRODUCTION AND EPIDEMIOLOGY

Headache is the fifth most common symptom presenting to the ED in the United States, with a total of 2.1 million visits per year.[1] Overall, headaches affect people across all ethnic, geographic, and economic levels, with an estimated global prevalence of 47% in adults.[2]

In the ED, the approach to headache focuses on identifying patients at risk for rapid deterioration, morbidity, and mortality; rapidly identifying high-risk headache syndromes; and providing appropriate headache therapy.

PATHOPHYSIOLOGY

The brain parenchyma has no pain sensors.[3] Early theories postulating vasoconstriction and rebound vasodilatation as the cause of migraine have been refuted.[4] Numerous physiologic mechanisms play a role in the development of the various clinical headache syndromes. For example, occipital nerve irritation may lead to the development of occipital neuralgia.[5] Similarly, headaches associated with disturbances in intracranial pressure (both high and low) are related to compression of, or traction on, pressure-sensitive structures in the meninges.[6] The pathophysiologic mechanisms of other headache syndromes, such as migraine headaches, cluster headaches, and toxic and metabolic headaches, are less clear. Discussion of these mechanisms is beyond the scope of this chapter.

CLINICAL FEATURES

Most patients with headache have conditions that are painful but benign in etiology. Identifying those at high risk is the first step in management (Table 165-1). A high-risk cause for headache accounts for only 4% of all headaches but 10% to 14% of acute-onset ("thunderclap") headaches.[7,8]

Although headaches are typically classified as **primary headaches** when there is no underlying cause (such as migraine or cluster headaches) and **secondary headaches** if associated with an underlying cause (such as tumor, meningitis, or subarachnoid hemorrhage), this distinction is not clinically useful in the ED setting.

TABLE 165-1

High-Risk Features for Headache: Clinical "Red Flags"

Onset	Sudden Trauma Exertion
Symptoms	Altered mental status Seizure Fever Neurologic symptoms Visual changes
Medications	Anticoagulants/antiplatelets Recent antibiotic use Immunosuppressants
Past history	No prior headache Change in headache quality, or progressive headache worsening over weeks/months
Associated conditions	Pregnancy or postpregnancy status Systemic lupus erythematosus Behçet's disease Vasculitis Sarcoidosis Cancer
Physical examination	Altered mental status Fever Neck stiffness

	Papilledema Focal neurologic signs

HISTORY

Features associated with high-risk headaches are as follows:

Patient Age

Patients >50 years of age, with a new or worsening headache, represent a high-risk group. The incidence of migraine, cluster, and tension headaches decreases with age, raising the likelihood of ominous pathology for older patients.[9]

Onset of Symptoms

The abrupt onset of severe headache, or **"thunderclap" headache**, requires immediate and thorough evaluation.[10] Thunderclap headache associated with intracerebral aneurysmal leak ("sentinel hemorrhage" or "herald bleed") may precede catastrophic aneurysmal rupture. Associated symptoms may include neck stiffness, nausea, vomiting, loss of consciousness, neurologic deficit, or altered mentation.[11] Onset of thunderclap headache during periods of exertion raises suspicion for subarachnoid hemorrhage or **arterial dissection** of the carotid or vertebrobasilar circulation. Headaches associated with the Valsalva maneuver may herald an intracranial abnormality.[12] Rarely, spontaneous intracranial hypotension and acute hydrocephalus associated with third ventricular colloid cyst may present with thunderclap headache.[13] Other causes for thunderclap headache are listed in Table 165-2.

TABLE 165-2

Causes of Thunderclap Headache

Hemorrhage	Intracranial hemorrhage "Sentinel" aneurysmal hemorrhage Spontaneous intracerebral hemorrhage
Vascular	Carotid or vertebrobasilar dissection Reversible cerebral vasoconstriction syndrome (RCVS) Cerebral venous thrombosis Posterior reversible encephalopathy syndrome (PRES)
Other causes	Coital headache Valsalva-associated headache Spontaneous intracranial hypotension Acute hydrocephalus (e.g., colloid cyst obstructing third ventricle)[13] Pituitary apoplexy

Headache Quality

A change in pattern, frequency, quality, or intensity of a preexisting headache syndrome needs the same evaluation as a new-onset headache syndrome.

Fever

Fever raises concern for CNS infection, such as meningitis, encephalitis, or brain abscess. However, the absence of fever does not exclude a CNS infection, especially in patients at the extremes of age and with immunocompromised states.

Medication History

Ask about over-the-counter medications, anticoagulants, antiplatelet agents, chronic steroids, immunomodulatory agents, or antibiotics (prescribed or not) to identify patients at high risk for infection (e.g., eculizumab and its elevated risk for meningococcal infection). Chronic use of analgesic and anti-inflammatory agents may result in **rebound or withdrawal headaches**. Medication overuse is defined as use >10 times a month and is notable for ergots, triptans, and opioids.[12] Anticoagulants and antiplatelet agents increase the risk for hemorrhage, both spontaneous and traumatic.[14] The recent use of antibiotics may present with a falsely reassuring clinical appearance due to partial treatment of a potentially dangerous CNS infection.

Prior Headache History

A prior history suggestive of migraine, tension, or cluster-type headaches, and response to specific therapy, may obviate the need for extensive ED evaluation (**Tables 165-3 and 165-4**).

TABLE 165-3

Clinical Features Suggestive of Migraine

Prior history of migraine	Moderate/severe intensity
Younger age	Unilateral
Multiple prior episodes	Throbbing
Aura and prodrome	Nausea/vomiting
Familiar triggers	Photophobia/phonophobia
Family history	Lasts hours
History of motion sickness	

TABLE 165-4

Clinical Features Suggestive of Cluster Headache

At least 5 attacks that meet the following criteria: • Severe • Unilateral • Lasts 15–180 min (untreated) • Circadian/circannual pattern	Associated **ipsilateral symptoms** (at least one): • Lacrimation • Conjunctival injection • Nasal congestion or rhinorrhea • Ptosis and/or miosis • Edema of the eyelid and/or face • Sweating of the forehead and/or face

Substance Use History

Use of adrenergic agents such as cocaine, amphetamine, or derivative compounds such as methamphetamine increases risk of intracranial hemorrhage or the less common entity of reversible cerebral vasoconstriction syndrome.[15] Patients with a history of alcohol abuse are at increased risk of intracranial bleeding due to falls, interpersonal violence, and the potential for liver dysfunction associated with prolonged coagulation times and thrombocytopenia.

Family History

Known aneurysm or sudden death in first-degree relatives raises the suspicion for intracranial aneurysm.[16] The incidence of aneurysm in patients with a family history is three to five times higher than in those without a family history. A personal or family history of autosomal dominant polycystic kidney disease also increases the risk for intracranial aneurysm. In patients with autosomal dominant polycystic kidney disease, aneurysmal rupture is more likely to occur at a younger age. The presence of migraine in a first-degree relative is associated with a two- to four-fold increased risk of developing migraine.[17]

PHYSICAL EXAMINATION

Vital Signs

Headache is a common symptom associated with fever. For example, headache is seen in up to 60% of patients with upper respiratory tract infection symptoms.[7,18] However, the persistence of headache in the presence of a normalized temperature suggests consideration for further evaluation of a possible CNS infection. The presence of fever in association with neck stiffness and altered mental status represents the classic triad of meningitis. Ninety-five percent of patients with bacterial meningitis present with at least two of the four findings (classic triad plus headache).[19]

Severe hypertension can be associated with headache and the development of acute changes in mental status and neurologic function. Posterior reversible encephalopathy syndrome[20] and hypertensive urgency should be considered in such patients (see "Posterior Reversible Encephalopathy Syndrome" section).

Examination of the Head and Neck

Meningismus is an important clinical clue to the presence of infection or hemorrhage.[19] Examine the ears, nose, and throat to identify otitis media and sinusitis, both of which may cause headache and contribute to the extension of infection to the CNS. Palpate for scalp tenderness and tenderness over the temporal arteries to assess for possible temporal arteritis.

Examination of the Eye

Headache can occur with acute angle-closure glaucoma, scleritis, and endophthalmitis. Consider **acute angle-closure glaucoma** even when there is no focal ocular complaint, because the pain can be so severe the patient may fail to localize pain to the eye. Measure intraocular pressure to exclude glaucoma. Check visual acuity and visual fields and examine the pupils and eyelids, checking for signs of Horner's syndrome.

Funduscopic Examination

Papilledema can be seen in the presence of raised intracranial pressure. However, there is typically a delay in the onset of papilledema once intracranial pressure begins to elevate, and papilledema can persist once intracranial pressure returns to normal.[21] The ability to recognize papilledema by routine direct ophthalmoscopy alone (particularly with nondilated pupils) is limited, but using a panoptic ophthalmoscope provides a more reliable view of the retina.[22] Bedside US of the optic nerve sheath can also assess for papilledema.[23,24] The presence of papilledema requires CT imaging before lumbar puncture.[25]

Neurologic Examination

A baseline neurologic assessment includes the following: mental status assessment; cranial nerve examination, including pupillary examination (for asymmetry or ptosis, which may suggest third nerve compression by posterior communicating artery aneurysms); assessment for other cranial neuropathies (which may raise suspicion for carcinomatous meningitis); motor examination to detect extremity weakness (particularly subtle weakness with pronator drift); reflex examination for subtle asymmetry or a Babinski reflex; and gait and coordination testing (which may be impaired in cerebellar lesions).

DIAGNOSIS

There are many causes of headache, each of which is diagnosed and managed differently. See discussions of specific causes of headache below.

LABORATORY TESTING

Routine blood testing is of limited utility in the diagnosis of acute headache and should be guided by the patient's age, history, relevant comorbidities, and medication history.

The laboratory evaluation of patients with high-risk headaches may include basic metabolic profile, CBC, coagulation panel, erythrocyte sedimentation rate, and blood cultures for possible infection.

IMAGING

Selecting an appropriate imaging study depends on the history, physical examination findings, and differential diagnosis of headache,[26,27,28] as well as the resources available to the emergency provider. Table 165-5 summarizes some of the American College of Radiology recommendations for appropriate imaging. When MRI is immediately unavailable and diagnostic uncertainty regarding the possibility of an underlying lesion prevails, further imaging may be necessary, the timing of which will depend on the clinical circumstances and likelihood of the patient being able to follow-up in a reliable fashion.[26]

TABLE 165-5

Choice of Imaging Modality

Noncontrast Head CT	MRI of Brain With and Without Contrast
• Trauma • Thunderclap headache • New headache *plus* focal neurologic deficit or papilledema • Chronic headache *plus* change in clinical features*	• New-onset headache *plus* focal neurologic deficit/papilledema • Possible encephalitis • Possible vertebral/carotid dissection • Horner's syndrome • Valsalva or coital headache • Immunocompromised individual • Patient with cancer history/current cancer • Suspected temporal arteritis • Intracranial hypotension (low-pressure headache) • Headache with suspected intracranial complication of sinusitis/mastoiditis/oromaxillofacial origin • New-onset headache in pregnant woman (without contrast) • Headache of trigeminal autonomic origin • Chronic headache with *new* feature or focal deficit (CT can be first step)

If the patient presents with a typical history of headache that responds to typical measures and a normal neurologic examination, avoiding imaging may be prudent to reduce the risk for radiation exposure. For most patients in the ED with headache, a noncontrast head CT is the fastest and most appropriate initial imaging study, as well as the most sensitive for detecting acute intracranial hemorrhage.[28,29]

Contrast (iodinated contrast and gadolinium-based magnetic resonance contrast agents) is contraindicated for patients with renal insufficiency due to risk for renal toxicity and nephrogenic systemic fibrosis.[30] Gadolinium is also relatively contraindicated in pregnancy and breastfeeding women. MRI can be limited by claustrophobia. A discussion with the radiologist and/or radiology technical staff can clarify the safety of MRI in patients with devices or foreign bodies.

Magnetic resonance angiography is useful in detecting arterial disease (stenosis, congenital anomalies, dissection, CNS vasculitis) and should be considered in any case where there may be arterial pathology underlying the patient's symptoms. Discuss concerns for dissection with the radiologist to determine the most appropriate MRI method.

If MRI is unavailable or not clinically feasible, consultation with radiology regarding other appropriate imaging modalities is prudent.

LUMBAR PUNCTURE

After the clinical assessment, blood work, and imaging, the next step is to determine whether or not to perform a lumbar puncture (LP) and, if so, the timing of LP. LP can serve as both a diagnostic tool (as in meningitis, subarachnoid hemorrhage, intracranial hypotension, carcinomatous meningitis) and therapeutic tool (as in pseudotumor cerebri).

Ideally, perform the LP with the patient in the lateral decubitus position in order to allow for the accurate measurement of opening pressure. Seated LP does not allow for accurate assessment of opening pressure. Opening pressure provides critical information about the patient's intracranial pressure, should be performed routinely, and should be considered a routine procedure when performing LP.

The possibility of herniation in association with LP is a frequent concern of emergency providers. There is no randomized controlled trial assessing the question of when it is safe to perform an LP. The cumulative evidence suggests that in patients without a history of immunosuppression, who have a normal sensorium, and who have no focal neurologic deficits, it is safe to proceed with LP without imaging prior to LP.[31,32]

In the evaluation of patients with suspected acute bacterial meningitis, clinical signs of "impending" herniation are the best predictors of when to delay an LP because of the risk of precipitating herniation. Risk of an abnormal CT scan is elevated in patients with any of the following clinical features: a deteriorating or altered level of consciousness (particularly a Glasgow coma scale score of ≤11), brainstem signs (including pupillary changes, posturing, or irregular respirations), focal neurologic deficit, history of recent seizure, history of a preexisting neurologic disorder, or history of immunocompromised state. In patients with these clinical features, imaging prior to LP is appropriate, but antibiotic administration should not be delayed while imaging is obtained. In patients without such findings, it is usually safe to perform LP without performing a CT scan in cases of suspected bacterial meningitis.[33]

DISPOSITION AND FOLLOW-UP

Most patients with headache can be treated and released from the ED with an appropriate follow-up plan. Identification of potential barriers to follow-up is an important step in ensuring that proper follow-up will be available to all patients, particularly for patients with limited resources or other barriers to accessing medical care. For some patients, inpatient care or observation may be warranted until symptoms improve or until testing is completed. A follow-up plan is especially important for patients with high-risk conditions, such as temporal arteritis or idiopathic intracranial hypertension. Follow-up is similarly important for patients with chronic headaches, given the potential for substance abuse, overutilization of resources, and repeated unnecessary imaging with potentially harmful radiation.[27]

SPECIFIC CAUSES OF HEADACHE

MENINGITIS

Consider meningitis in patients with headache and the classic triad of fever, altered mentation, and neck stiffness.[19] The source of infection can be viral, bacterial, and less commonly, fungal or parasitic. Have a high index of suspicion for meningitis in those with immunosuppression (particularly acquired immunodeficiency syndrome, human immunodeficiency virus, cancer history, chemotherapy, chronic steroids), which may be associated with more insidious types of meningitis such as *Cryptococcus*. An LP is indicated for suspected meningitis. **If the LP is delayed (e.g., CT, coagulopathy, thrombocytopenia, agitation) and meningitis is strongly suspected, administer antibiotics without delay.**[25,34] For many patients who are awake, are alert with no evidence of papilledema or focal neurologic deficit, and have no history to suggest immunocompromised state or new-onset seizure, the head CT can be delayed until after the LP.[25]

SUBARACHNOID HEMORRHAGE

Subarachnoid hemorrhage resulting from rupture of an intracranial aneurysm carries only a 50% 30-day survival rate.[35,36] Approximately half of survivors have some degree of neurologic impairment. Early detection and appropriate management lead to improved clinical outcome. Only 1% of patients presenting to the ED with headache have subarachnoid hemorrhage. However, 10% to 14% of those complaining of the "worst headache of their life" have subarachnoid hemorrhage.[7,8] **Acute onset of a severe headache is subarachnoid hemorrhage until proven otherwise.**[10,11] Inquire about a family history as outlined above.[16] Obtain a noncontrast head CT as the first step in evaluation.[37] With third–generation CT equipment, CT scan done within 6 hours of headache onset is reported to have a sensitivity of 93% and specificity of 100%, with a negative predictive value of 99.4% and positive predictive value of 100%.[38] If head CT is negative for blood but suspicion for subarachnoid hemorrhage is strong, the next step is LP to detect blood or xanthochromia in the cerebrospinal fluid.[39] For further discussion, see chapter 166, "Spontaneous Subarachnoid and Intracerebral Hemorrhage." Consultation with a neurologist or neurosurgeon may be appropriate if the history

is highly suggestive of subarachnoid hemorrhage, because both the CT and LP can be normal.[40,41,42] CT angiogram, magnetic resonance angiogram, MRI with fluid-attenuated inversion recovery/susceptibility-weighted images,[43,44] or four-vessel cerebral angiogram may be reasonable.[26]

SUBDURAL HEMATOMA AND INTRACEREBRAL HEMORRHAGE

Intracranial hemorrhage may occur with or without a history of trauma, in the context of new or progressive headache, with or without associated neurologic deficit. This is particularly important in the elderly, those with chronic alcohol and substance abuse, and patients using antiplatelet and anticoagulant agents. The antiplatelet agent clopidogrel increases the risk of acute intracranial bleeding immediately after trauma, so patients receiving antiplatelet agents and anticoagulants should be screened using head CT, regardless of symptoms. In a prospective trial of patients with blunt head trauma, 12% of those taking clopidogrel and 5.1% of those taking warfarin had acute intracranial hemorrhage noted on their initial CT scan. The risk of delayed intracranial hemorrhage was small in both groups (0 of 296 patients taking clopidogrel and 4 of 687 patients taking warfarin).[14]

Acute headache with associated vestibular symptoms (vertigo or ataxia) should be considered a cerebellar hemorrhage until proven otherwise. Cerebellar hemorrhages make up approximately 10% of all intracerebral hemorrhages and may require prompt surgical evacuation of the hematoma in order to prevent the rapid progression to severe disability or death.[45]

BRAIN TUMOR

Headache in the setting of brain tumor is caused, at least in part, by cerebrospinal fluid flow obstruction and intracranial hypertension.[46]

Clinical signs and symptoms suggesting brain tumor include abnormal neurologic examination, headache worsened by Valsalva maneuver, headache causing awakening from sleep, seizures, recent cancer diagnosis, or mental status change. Of course, the absence of these features does not exclude the possibility of a brain tumor. MRI with and without gadolinium is the study of choice for detecting brain tumors, but cost and limited access make it unfeasible in many settings. A noncontrast CT will identify large masses and edema associated with large masses, but may fail to identify smaller masses. Evaluate for potential barriers to access of medical care in clinical decision making, because additional imaging may be needed at follow-up.

CEREBRAL VENOUS THROMBOSIS

Cerebral venous thrombosis is a rare, but dangerous, cause of headache. Consider the diagnosis in patients presenting with new headache symptoms, especially in the presence of certain known risk factors. Cerebral venous thrombosis is more common in women, especially in the peripartum period, and in patients with a recent surgical history. It is associated with hypercoagulable states such as use of oral contraceptives, hematologic disorders, factor V Leiden homozygous mutation, protein S or protein C deficiency, and anti–thrombin III deficiency.[47] The presentation can vary widely, from a progressive headache developing over days to weeks to, in some instances, a "thunderclap" headache. Similarly, the patient's clinical appearance can be quite benign, especially early on in the course of the illness, or in more severe cases, patients may present with seizures, stroke symptoms, and even coma.[48,49]

In the presence of abnormal imaging (CT, MRI), focal neurologic deficit, or altered mental status, the diagnosis is made definitively with magnetic resonance venography. Given the rare nature of this diagnosis, it is likely that patients suffering from cerebral venous thrombosis may be undergoing evaluation for other causes of severe headache. An elevated LP opening pressure should raise suspicion of central venous thrombosis in the appropriate clinical setting and prompt further imaging with magnetic resonance venography or consultation with a neurologist.[50,51] LP can safely be performed in patients with central venous thrombosis.

POSTERIOR REVERSIBLE ENCEPHALOPATHY SYNDROME (PRES)

Patients with posterior reversible encephalopathy syndrome can present with severe headache, visual changes, seizures, and encephalopathy in the setting of marked blood pressure elevation (usually rapidly developing). It is most common in patients undergoing active treatment with immune-suppressing or modulating medications or chemotherapeutic agents, as well as in patients with end-stage renal disease. Imaging with MRI typically shows evidence of symmetrical vasogenic edema in the occipital area of the brain, although other areas of the brain can be involved. Treatment involves blood pressure control and supportive care.[52]

REVERSIBLE CEREBRAL VASOCONSTRICTION SYNDROME

This condition is one of a short list of conditions that can mimic subarachnoid hemorrhage (Table 165-2). Characterized by the occurrence of one or more "thunderclap" headaches, the diagnosis should only be considered when the evaluation for subarachnoid hemorrhage has proven negative. The underlying pathophysiology of the syndrome is poorly understood, but it appears to coexist with a number of other cerebral angiopathies (including posterior reversible encephalopathy syndrome) that are characterized by diffuse cerebral vasospasm. The incidence is greater in women, and the peak age of onset is in the early 40s. Most patients will have more than one thunderclap headache over the course of a few weeks. Severe headache may be the only presenting feature, although some patients can present with seizure or focal neurologic deficit. The key diagnostic feature (multiple areas of cerebral vasoconstriction on cerebral angiography) is most commonly found on follow-up angiography

between 2 and 3 weeks after symptom onset.[15] In three published series, the rate of permanent neurologic disability was between 6% and 20%. Reversible cerebral vasoconstriction syndrome, although not widely known among nonneurologists, does not appear to be that rare. One prospective case series included 67 patients diagnosed at a single hospital over a 3-year period of data collection.[53,54]

Initial neuroimaging in these patients may show evidence of non-aneurysmal subarachnoid hemorrhage, ischemic stroke, or intracranial hemorrhage. However, head CT is most commonly normal in these patients. Ultimately, there will be magnetic resonance angiography evidence of cerebral vasoconstriction in all patients, but this may be delayed in appearance. As such, the clinical presentation of thunderclap headache without evidence of subarachnoid hemorrhage should be the main prompt to making this diagnosis or consulting with a neurologist.

TEMPORAL ARTERITIS

Temporal arteritis, also known as giant cell arteritis, is an inflammatory condition affecting the small and medium-sized intracranial and extracranial vessels. Primarily a disease of those >50 years old, its incidence increases with age. In addition to headache, associated symptoms may include fatigue, fever, proximal muscle weakness, jaw claudication, or transient ischemic attack symptoms, especially transient visual loss. Sedimentation rate may be elevated. Check intraocular pressure to exclude glaucoma. Diagnosis is made by the presence of three of the five criteria listed in Table 165-6, with a sensitivity of 93.5% and a specificity of 91.2%.[55] Begin treatment with prednisone, 60 milligrams PO daily, to minimize morbidity from visual impairment and stroke. Consult with an ophthalmologist to determine optic nerve function and a rheumatologist. It is important to ensure that there is rapid and appropriate follow-up for patients discharged from the ED, ideally with their primary care provider.

TABLE 165-6

American College of Rheumatology Criteria for Diagnosis of Temporal Arteritis

Clinical Features	Comments
Age at disease onset ≥50 years	
New headache	Onset or type
Temporal artery abnormality	Tenderness to palpation of temporal arteries Decreased pulsation of temporal arteries
Erythrocyte sedimentation rate ≥50 mm/h	Westergren method
Abnormal artery biopsy (can be done after initiating steroids)	Vasculitis Predominance of mononuclear cell infiltration or granulomatous inflammation Multinucleated giant cells

MIGRAINE

The most common non–life-threatening headache in the ED is **migraine** (Table 165-3). Migraine is defined as a headache of moderate to severe intensity that lasts hours (4 to 72 hours on average) and is usually unilateral, pulsatile in quality, typically associated with both photophobia and phonophobia, and generally made worse with physical activity. Migraine can be episodic or chronic and can occur with or without aura. The characteristics of migraine aura vary widely. Among the most common aura symptoms are lightheadedness and visual changes (scotoma and scintillations). Migraines usually start in childhood and peak around age 40 years, with gradual decline thereafter. Prevalence is about 5% for males and 15% to 17% for females.[9]

Chronic migraine is defined as 5 or more migraine headache days per month over the past 3 months. Migraine sufferers who present to the ED are more likely to be chronic headache sufferers.[56,57]

There are many effective treatment options for management of migraine headache, based on randomized controlled trials. Triptans are considered first-line abortive therapy for migraine. However, in the ED setting, most patients have failed abortive therapy and require rescue therapy.

ED Treatment of Migraine

Initial treatment consists of IV hydration and repetitive IV treatment with nonsteroidal anti-inflammatory drugs and an antiemetic (Table 165-7). Many combinations are effective. **Combination with antihistamine (usually diphenhydramine 25 to 50 milligrams IV) is helpful,** because increased histamine levels correlate with migraine attacks, and diphenhydramine can also treat akathisias from antiemetics. Antihistamines alone are not helpful.[58]

TABLE 165-7

Treatment Options for Migraine Headache

Drug	Dosing	Contraindications	Precautions and Pregnancy Category	Notes
Ketorolac	30 milligrams IV or IM	History of peptic ulcer disease (especially in elderly)	Pregnancy Category B Avoid in third trimester	
Prochlorperazine	5–10 milligrams IV or PR		Pregnancy Category C Drowsiness Dystonic reactions	**Antiemetic** Concurrent: diphenhydramine
Metoclopramide	10 milligrams IV		Pregnancy Category B Drowsiness Dystonic reactions	**Antiemetic** Concurrent: diphenhydramine
Droperidol	2.5 milligrams IV slow, or 2.5 milligrams IM		Pregnancy Category C QT interval prolongation and/or torsade de pointes	Concurrent: diphenhydramine
Chlorpromazine	7.5 milligrams IV		Pregnancy not classified Hypotension Drowsiness Dystonic reactions	**Antiemetic** Pretreat with: normal saline bolus to minimize hypotension Concurrent: diphenhydramine
Magnesium sulfate	2 grams IV over 30 min		Pregnancy Category D but effective in pre-eclampsia and eclampsia	Nonvalidated

Drug	Dosing	Contraindications	Precautions and Pregnancy Category	Notes
Methylprednisolone	125 milligrams IV or IM		Rescue therapy	Nonvalidated
Dexamethasone	6–10 milligrams IV		Rescue therapy	Adjunctive therapy to reduce recurrence
Sumatriptan	6 milligrams SC	Ischemic Heart Disease Uncontrolled hypertension Basilar or hemiplegic migraine	Pregnancy Category C	
Dihydroergotamine (DHE)	1 milligram IV over 3 min	Pregnancy Uncontrolled hypertension Ischemic Heart Disease Recent sumatriptan use (within 24 h)[61] Basilar or hemiplegic migraine	Pregnancy Category X Nausea Vomiting Diarrhea Abdominal pain	Pretreat with antiemetic
Valproate	500 milligrams IV	Pregnancy	Pregnancy Category X	Nonvalidated

Steroids can be useful to reduce the risk for headache recurrence after ED discharge.[59,60]

Opiates and barbiturate-containing compounds should not be used routinely for abortive migraine therapy unless other standard treatments fail. Not recommended for routine use are ergotamine and codeine- and tramadol-containing medications, as well as butorphanol and butalbital-containing medications.[62,63]

In **pregnancy**, there is scant data on treatment of migraine. In general, triptans are contraindicated; acetaminophen, opioids, or corticosteroids can be used. Metoclopramide (U.S. Food and Drug Administration Category B) may be used. Nonsteroidal anti-inflammatory drugs may be also used until the third trimester. Ergotamines and combination agents with caffeine and isometheptene are absolutely contraindicated in pregnant women.

Upon discharge from the ED, more than half of patients will have some residual headache, and there is an increased rate of recurrence of headache within the first 3 days after discharge.[59,60,64] Therefore, a prescription for abortive medications should form part of the discharge plan for patients being discharged from the ED with a diagnosis of migraine. Providers should be familiar with one or two fast-acting triptans (such as sumatriptan, sold as Imitrex™ in the United States, and rizatriptan, sold as Maxalt™ in the United States), as well as combinations of triptans, such as sumatriptan/naproxen (sold as Treximet™ in the United States), or combination drugs, such as Midrin™ (acetaminophen, 325 milligrams/dichloralphenazone, 100 milligrams/isometheptene, 65 milligrams).

OCCIPITAL NEURALGIA

Occipital neuralgia is characterized by paroxysms of lancinating pain at the back of the head, in the distribution of the greater and/or lesser occipital nerve. Patients describe the pain as stabbing or electric shock–like in quality, with hypersensitivity in the distribution of the affected nerve. Most cases are attributed to chronic neck tension or unknown causes. However, the condition can be associated with osteoarthritis or degenerative disease of the upper cervical spine. Occipital nerve block typically results in marked improvement of symptoms, and the results can persist for weeks after the injection. The procedure is both diagnostic and therapeutic. The procedure can be performed with ease in any setting and requires minimal expertise.

IDIOPATHIC INTRACRANIAL HYPERTENSION (PSEUDOTUMOR CEREBRI SYNDROME)

Idiopathic intracranial hypertension, also known as pseudotumor cerebri, is most common in obese women. The incidence is 19.3 per 100,000 obese women between the ages of 20 and 44 years and has increased along with the obesity epidemic. The most prominent symptoms include headache (84%), transient visual obscurations (68%), back pain (53%), and pulsatile tinnitus (52%). Only 32% of patients report visual loss. Untreated, idiopathic intracranial hypertension can lead to permanent visual impairment if not recognized and treated appropriately.[65]

The diagnostic criteria include papilledema with an otherwise normal neurologic examination and elevated opening pressure on LP (>25 cm H_2O in adults and >28 cm H_2O in children), in the setting of normal cerebrospinal fluid composition and normal imaging (having excluded other causes of raised intracranial pressure). Treatment is focused on preservation of vision. A variant of pseudotumor has been identified that does

not present with papilledema but may present with the other clinical features of pseudotumor cerebri, along with abducens nerve palsy (unilateral or bilateral). In the absence of either papilledema or abducens nerve palsy, the diagnosis of pseudotumor without papilledema can be made if at least three of the following neuroimaging findings are present: empty sella, flattening of the posterior aspect of the globe, distention of the perioptic subarachnoid space with or without a tortuous optic nerve, and transverse venous sinus stenosis.[66]

LP is necessary to make the diagnosis of idiopathic intracranial hypertension, and concomitant removal of a volume of cerebrospinal fluid can provide temporary relief of symptoms. However, subjective improvement of symptoms after LP is not reliable in establishing the diagnosis.[66] Perform the LP with the patient in the lateral decubitus position, without sedation (which may cause mild hypercapnia and, subsequently, an elevated cerebrospinal fluid pressure measurement). The knees should be extended for measurement of cerebrospinal fluid pressure, and the base of the manometer should be level with the right atrium. Elevated cerebrospinal fluid pressures can occur in the setting of the Valsalva maneuver, such as breath holding and crying, and if the pressure is measured in the sitting position. Cerebrospinal fluid can be removed in multiple aliquots, measuring cerebrospinal fluid pressure after each removal, until a target pressure of 15 to 20 cm H_2O is achieved. Determine the opening pressure. **In general, removal of 1 mL of cerebrospinal fluid will lower the cerebrospinal fluid pressure by about 1 cm H_2O.**[67] To avoid lowering the pressure excessively, first remove 1 mL for every 1 cm H_2O reduction desired, and then remeasure cerebrospinal fluid pressure. Excess cerebrospinal fluid removal can result in intracranial hypotension and a "low-pressure headache," which may require epidural blood patch for relief.

Oral acetazolamide can be effective in lowering intracranial pressure and decreasing the symptoms of idiopathic intracranial hypertension. Treatment is typically started at 250 to 500 milligrams twice a day.[68] The dose can be increased to as much as 4 grams/d, but dose escalation is associated with significant side effects (paresthesias, fatigue, decreased libido, metallic taste) and should be done under the supervision of a neurologist or ophthalmologist for ongoing monitoring of papilledema and visual field testing to minimize the risk of visual loss.[69] Long-term interventional management may include cerebrospinal fluid shunting and optic nerve sheath fenestration for failing vision. For obese patients, weight loss is recommended.[69]

INTRACRANIAL HYPOTENSION

The headache of intracranial hypotension (low-pressure headache) is most commonly associated with recent dural penetration, either during LP, epidural anesthesia, or any operative procedure that involves opening the dura. Using a noncutting needle reduces the risk of post-LP headache.[70] Rarely, intracranial hypotension can occur spontaneously or in association with head or spine trauma.[71,72,73] Clinical features include headache that increases in severity with upright posture but improves or resolves in the supine position. Associated symptoms, such as

alterations in hearing or vision, nausea, vomiting, diplopia, and visual changes, may occur. MRI, with and without contrast, confirms the diagnosis by showing diffuse enhancement of the meninges. The LP, if performed, should have an opening pressure <6 cm H_2O. Most patients experience spontaneous resolution of their symptoms. Evidence to support treatments, including IV fluid resuscitation and IV caffeine, is limited. The most effective therapy for low-pressure headache is an epidural blood patch, typically performed by anesthesiologists.[71,74]

CARCINOMATOUS MENINGITIS

About 5% to 10% of patients with cancer develop leptomeningeal metastases. In addition to headache, cranial nerve abnormalities (typically more than one) and other neurologic findings may be present. Risk factors for carcinomatous meningitis include aggressive lymphoma subtypes and uncontrolled systemic disease. In suspected patients, the appropriate testing would include MRI with and without contrast (to evaluate for meningeal enhancement). Obtain MRI before LP because MRI evidence of meningeal enhancement is common after LP and may confound the diagnosis. LP may reveal an elevated opening pressure (>20 cm H_2O). Cerebrospinal fluid analysis should include cytology (solid tumors) or flow cytometry (hematologic tumors). Malignant cells degrade quickly, so timely review of cerebrospinal fluid is important.[75]

CLUSTER HEADACHE

Cluster headaches (Table 165-4) occur in about 0.4% of the general population and can mimic dental pain. More common in men, cluster headaches typically start in adulthood and tend to occur in "clusters," with a circadian and circannual pattern, recurring daily for more than a week and remitting for at least 4 weeks. Episodes are typically unilateral and excruciating, but brief and self-limited. Up to 10% of patients will experience a more chronic form, with fewer episodes of remission. Associated **ipsilateral symptoms are common** (Table 165-4), and a distinguishing feature of this headache is the need for the patient to "pace," in contrast to the patient with migraine, who prefers to lie still in a quiet and dark room. Treatment consists of 100% oxygen administered at 12 L/min for 15 minutes through a nonrebreathing facemask.[76,77] Sumatriptan, 6 milligrams SC, can also be used.

HYPERTENSIVE HEADACHE

There is no compelling evidence linking mild to moderate **hypertension** with headache. Several studies using ambulatory blood pressure monitoring have found no association between mild to moderate high blood pressure (systolic blood pressure <180 mm Hg and/or diastolic blood pressure <120 mm Hg) and patient self-reported headache.[78] Uncontrolled hypertension can be associated with headache, especially in

conditions where there is a rapid and marked rise in blood pressure, such as pheochromocytoma, posterior reversible encephalopathy syndrome,[20] hypertensive crisis, pre-eclampsia, and eclampsia.[78]

METABOLIC CAUSES OF HEADACHE

Metabolic headaches are hallmarked by deterioration in the setting of a disorder of homeostasis and typically improve after resolution of the disorder of homeostasis (Table 165-8).[78]

TABLE 165-8

Metabolic Causes of Headache

History	Examples	Treatment
Hypoxia/hypercapnia	High altitude Air travel Pulmonary disease Congestive heart failure Sleep apnea	Acetaminophen/ibuprofen Acetazolamide 125–250 milligrams twice a day Steroids (dexamethasone) Prophylaxis: acetylsalicylic acid, 320 milligrams at 4-h intervals, starting 1 h prior to ascent; repeat 3 times Nonsteroidal anti-inflammatory drugs (NSAIDs), pseudoephedrine, and nasal decongestants
Dialysis		NSAIDs/analgesics during dialysis
Autonomic dysreflexia (typical in quadriplegia)		Seated position Remove/loosen clothing Scrutinize for bladder distension/bowel impaction
Other	Hypothyroidism Fasting Cardiac cephalgia (associated with myocardial ischemia)	

COITAL HEADACHE

Coital headache, also known as orgasmic headache, is a thunderclap headache that occurs at orgasm. Coital headache is considered benign with no specific treatment needed. Recovery is complete. However, the diagnosis is one of exclusion, to ensure that other causes of thunderclap

headache are not missed, including subarachnoid hemorrhage and reversible cerebral vasoconstriction syndrome.[79] The clinical diagnosis of coital headache is one of exclusion and cannot be made without imaging. If MRI is unavailable or not clinically feasible, consultation with radiology regarding other appropriate imaging modalities is prudent.[26]

VALSALVA-ASSOCIATED HEADACHE

Valsalva maneuver may trigger thunderclap headache, a diagnosis made when the headache is only associated with cough, straining, or a Valsalva maneuver, with normal neuroimaging. Symptomatic cough headache is the diagnosis made when an underlying pathology (usually a type I Chiari malformation) is likely to be the cause of the headache.[80]

PITUITARY APOPLEXY

Pituitary tumor apoplexy is a rare clinical diagnosis, that is usually due to spontaneous hemorrhage or infarction of a preexisting pituitary adenoma.[81] The earliest symptom is sudden, severe headache. The headache location tends to be retro-orbital, bifrontal, or suboccipital. Between 63% and 100% of patients will experience headache.[81] Associated symptoms may include ophthalmoplegia, reduced visual acuity, visual field defects, altered consciousness, meningismus, and nausea and vomiting. CT (noncontrast) and MRI may show a sellar mass and hemorrhage. In the first 1 to 2 hours, the hyperacute hemorrhage may be easier to see on CT than MRI. Pituitary adenomas and cerebral aneurysms have a co-occurrence rate of 7.4%.[81] Pituitary tumor apoplexy requires immediate treatment with corticosteroids and urgent neurosurgical consultation. The treatment usually requires consultations from endocrinology, ophthalmology, and neurology with intensive care monitoring.

THIRD VENTRICLE COLLOID CYSTS

Colloid cysts of the third ventricle are a rare cause of acute neurologic deterioration and sudden death. The colloid cyst is usually congenital, slow growing, and benign, accounting for about 0.2% to 2% of all intracranial tumors, but it is the most common tumor of the third ventricle.[82] The usual clinical presentation is a history of severe paroxysmal and episodic attacks of (typically frontal) headache associated with nausea and vomiting. The presumptive cause is the intermittent obstruction of cerebrospinal fluid flow through the foramina of Monro with associated rapid increase in intracranial pressure.[83]

SINUSITIS

Classic features of purulent nasal discharge, nasal or facial congestion, hyposomia, or anosmia with or without fever, along with headache, ear pain or fullness, halitosis, and dental pain, allow for clinical diagnosis of **sinusitis**,[84] and treatment with antibiotics is warranted.

REFERENCES

1. Schappert SM: Ambulatory care visits to physician offices, hospital outpatient departments, and emergency departments: United States, 1996. *Ambul Outreach* 1998: 8, 1998.
[PubMed: 10346600]

2. http://www.who.int/mediacentre/factsheets/fs277/en/ (World Health Organization: October 2012, Fact Sheet no. 277: Headache disorders.) Accessed April 28, 2014.

3. Kunkle EC, Ray BS, Wolff HG: Studies on headache: the mechanisms and significance of the headache associated with brain tumor. *Bull N Y Acad Med* 18: 400, 1942.
[PubMed: 19312276]

4. Goadsby PJ, Lipton RB, Ferrari MD: Migraine—current understanding and treatment. *N Engl J Med* 346: 257, 2002.
[PubMed: 11807151]

5. Perelson HN: Occipital nerve tenderness; a sign of headache. *South Med J* 40: 653, 1947.
[PubMed: 20252372]

6. Schievink WI: Spontaneous spinal cerebrospinal fluid leaks and intracranial hypotension. *JAMA* 295: 2286, 2006.
[PubMed: 16705110]

7. Goldstein JN, Camargo CA Jr, Pelletier AJ et al.: Headache in United States emergency departments: demographics, work-up and frequency of pathological diagnoses. *Cephalalgia* 26: 684, 2006.
[PubMed: 16686907]

8. Perry JJ, Stiell IG, Sivilotti ML et al.: Clinical decision rules to rule out subarachnoid hemorrhage for acute headache. *JAMA* 310: 1248, 2013.
[PubMed: 24065011]

9. Vinson DR: Treatment patterns of isolated benign headache in U.S. emergency departments. *Ann Emerg Med* 39: 215, 2002.
[PubMed: 11867972]

10. Day JW, Raskin NH: Thunderclap headache: symptom of unruptured cerebral aneurysm. *Lancet* 2: 1247, 1986.
[PubMed: 2878133]

11. Dilli E: Thunderclap headache. *Curr Neurol Neurosci Rep* 14: 437, 2014.
[PubMed: 24643327]

12. https://www.icsi.org/_asset/qwrznq/Headache.pdf (Beithon J, Gallenberg M, Johnson K et al.: Institute for Clinical Systems Improvement: diagnosis and treatment of headache). Accessed July 30, 2014.

13. Mortimer AM, Bradley MD, Stoodley NG, Renowden SA: Thunderclap headache: diagnostic considerations and neuroimaging features. *Clin Radiol* 68: e101, 2013.
[PubMed: 23245274]

14. Nishijima DK, Offerman SR, Ballard DW et al.: Risk of traumatic intracranial hemorrhage in patients with head injury and preinjury warfarin or clopidogrel use. *Acad Emerg Med* 20: 140, 2013.
[PubMed: 23406072]

15. Ducros A: Reversible cerebral vasoconstriction syndrome. *Lancet Neurol* 11: 906, 2012.
[PubMed: 22995694]

16. Nahed BV, Bydon M, Ozturk AK, Bilguvar K, Bayrakli F, Gunel M: Genetics of intracranial aneurysms. *Neurosurgery* 60: 213, 2007.
[PubMed: 17290171]

17. Gardner KL: Genetics of migraine: an update. *Headache* 46 (Suppl 1): S19, 2006.
[PubMed: 16927960]

18. Eccles R: Understanding the symptoms of the common cold and influenza. *Lancet Infect Dis* 5: 718, 2005.
[PubMed: 16253889]

19. van de Beek D, de Gans J, Spanjaard L, Weisfelt M, Reitsma JB, Vermeulen M: Clinical features and prognostic factors in adults with bacterial meningitis. *N Engl J Med* 351: 1849, 2004.
[PubMed: 15509818]

20. Hinchey J, Chaves C, Appignani B et al.: A reversible posterior leukoencephalopathy syndrome. *N Engl J Med* 334: 494, 1996.
[PubMed: 8559202]

21. Steffen H, Eifert B, Aschoff A, Kolling GH, Volcker HE: The diagnostic value of optic disc evaluation in acute elevated intracranial pressure. *Ophthalmology* 103: 1229, 1996.
[PubMed: 8764791]

22. McComiskie JE, Greer RM, Gole GA: Panoptic versus conventional ophthalmoscope. *Clin Exp Ophthalmol* 32: 238, 2004.
[PubMed: 15180833]

23. Dubourg J, Messerer M, Karakitsos D et al.: Individual patient data systematic review and meta-analysis of optic nerve sheath diameter ultrasonography for detecting raised intracranial pressure: protocol of the ONSD research group. *Syst Rev* 2: 62, 2013.
[PubMed: 23919384]

24. Kimberly HH, Shah S, Marill K, Noble V: Correlation of optic nerve sheath diameter with direct measurement of intracranial pressure. *Acad Emerg Med* 15: 201, 2008.
[PubMed: 18275454]

25. Glimaker M, Johansson B, Bell M et al.: Early lumbar puncture in adult bacterial meningitis–rationale for revised guidelines. *Scand J Infect Dis* 45: 657, 2013.
[PubMed: 23808722]

26. Strain JD, Strife JL, Kushner DC et al.: Headache: American College of Radiology appropriateness criteria. *Radiology* 215 (Suppl): 855, 2000.
[PubMed: 11037510]

27. Loder E, Weizenbaum E, Frishberg B, Silberstein S: American Headache Society Choosing Wisely Task Force: Choosing wisely in headache medicine: the American Headache Society's list of five things physicians and patients should question. *Headache* 53: 1651, 2013.

[PubMed: 24266337]

28. Douglas AC, Wippold FJ 2nd, Broderick DF et al.: ACR appropriateness criteria: headache. *J Am Coll Radiol* 11: 657, 2014.
[PubMed: 24933450]

29. Gee C, Dawson M, Bledsoe J et al.: Sensitivity of newer-generation computed tomography scanners for subarachnoid hemorrhage: a Bayesian analysis. *J Emerg Med* 43: 13, 2012.
[PubMed: 22326408]

30. Sanyal S, Marckmann P, Scherer S, Abraham JL: Multiorgan gadolinium (gd) deposition and fibrosis in a patient with nephrogenic systemic fibrosis—an autopsy-based review. *Nephrol Dial Transplant* 26: 3616, 2011.
[PubMed: 21441397]

31. van Crevel H, Hijdra A, de Gans J: Lumbar puncture and the risk of herniation: when should we first perform CT? *J Neurol* 249: 129, 2002.
[PubMed: 11985377]

32. Canhao P, Abreu LF, Ferro JM et al.: Safety of lumbar puncture in patients with cerebral venous thrombosis. *Eur J Neurol* 20: 1075, 2013.
[PubMed: 23551518]

33. Hasbun R, Abrahams J, Jekel J, Quagliarello VJ: Computed tomography of the head before lumbar puncture in adults with suspected meningitis. *N Engl J Med* 345: 1727, 2001.
[PubMed: 11742046]

34. Brunell A, Ridefelt P, Zelano J: Differential diagnostic yield of lumbar puncture in investigation of suspected subarachnoid haemorrhage: a retrospective study. *J Neurol* 260: 1631, 2013.
[PubMed: 23358626]

35. Hop JW, Rinkel GJ, Algra A, van Gijn J: Case-fatality rates and functional outcome after subarachnoid hemorrhage: a systematic review. *Stroke* 28: 660, 1997.
[PubMed: 9056628]

36. Suarez JI, Tarr RW, Selman WR: Aneurysmal subarachnoid hemorrhage. *N Engl J Med* 354: 387, 2006.
[PubMed: 16436770]

37. Mayor S: Earlier diagnosis is needed to reduce deaths and disability from aneurysmal subarachnoid haemorrhage. *BMJ* 347: f6925, 2013.
[PubMed: 24270096]

38. Perry JJ, Stiell IG, Sivilotti ML et al.: Sensitivity of computed tomography performed within six hours of onset of headache for diagnosis of subarachnoid haemorrhage: prospective cohort study. *BMJ* 343: d4277, 2011.
[PubMed: 21768192]

39. Edlow JA, Malek AM, Ogilvy CS: Aneurysmal subarachnoid hemorrhage: update for emergency physicians. *J Emerg Med* 34: 237, 2008.
[PubMed: 18155383]

40. Heasley DC, Mohamed MA, Yousem DM: Clearing of red blood cells in lumbar puncture does not rule out ruptured aneurysm in patients with suspected subarachnoid hemorrhage but negative head CT findings. *AJNR Am J Neuroradiol* 26: 820, 2005.
[PubMed: 15814927]

41. Horstman P, Linn FH, Voorbij HA, Rinkel GJ: Chance of aneurysm in patients suspected of SAH who have a "negative" CT scan but a "positive" lumbar puncture. *J Neurol* 259: 649, 2012.
[PubMed: 21901483]

42. O'Laughlin KN, Hoffman JR, Go S et al.: Nonconcordance between clinical and head CT findings: the specter of overdiagnosis. *Emerg Med Int* 2013: 314948, 2013.
[PubMed: 24222854]

43. Frontera JA, Ahmed W, Zach V et al.: Acute ischaemia after subarachnoid haemorrhage, relationship with early brain injury and impact on outcome: a prospective quantitative MRI study. *J Neurol Neurosurg Psychiatry* April 8, 2014. [Epub ahead of print]

44. Verma RK, Kottke R, Andereggen L et al.: U.S. U.S. Detecting subarachnoid hemorrhage: comparison of combined FLAIR/SWI versus CT. *Eur J Radiol* 82: 1539, 2013.
[PubMed: 23632159]

45. Witsch J, Neugebauer H, Zweckberger K, Juttler E: Primary cerebellar haemorrhage: complications, treatment and outcome. *Clin Neurol Neurosurg* 115: 863, 2013.
[PubMed: 23659765]

46. Kahn K, Finkel A: It is a tumor: current review of headache and brain tumor. *Curr Pain Headache Rep* 18: 421, 2014.
[PubMed: 24760490]

47. Alvis-Miranda HR, Milena Castellar-Leones S, Alcala-Cerra G, Rafael Moscote-Salazar L: Cerebral sinus venous thrombosis. *J Neurosci Rural Pract* 4: 427, 2013.
[PubMed: 24347950]

48. Fischer C, Goldstein J, Edlow J: Cerebral venous sinus thrombosis in the emergency department: retrospective analysis of 17 cases and review of the literature. *J Emerg Med* 38: 140, 2010.
[PubMed: 20031365]

49. de Bruijn SF, Stam J, Kappelle LJ: Thunderclap headache as first symptom of cerebral venous sinus thrombosis. CVST study group. *Lancet* 348: 1623, 1996.
[PubMed: 8961993]

50. Iurlaro S, Beghi E, Massetto N et al.: Does headache represent a clinical marker in early diagnosis of cerebral venous thrombosis? A prospective multicentric study. *Neurol Sci* 25 (Suppl 3): S298, 2004.
[PubMed: 15549568]

51. Agostoni E: Headache in cerebral venous thrombosis. *Neurol Sci* 25 (Suppl 3): S206, 2004.
[PubMed: 15549538]

52. Lee VH: Clinical spectrum of reversible posterior leukoencephalopathy syndrome. *Arch Neurol* 65: 205, 2008.
[PubMed: 18268188]

53. Ducros A, Boukobza M, Porcher R et al.: The clinical and radiological spectrum of reversible cerebral vasoconstriction syndrome. A prospective series of 67 patients. *Brain* 130: 3091, 2007.

[PubMed: 18025032]

54. Ducros A, Boukobza M, Porcher R, Sarov M, Valade D, Bousser MG: The clinical and radiological spectrum of reversible cerebral vasoconstriction syndrome. A prospective series of 67 patients. *Brain* 130: 3091, 2007.
[PubMed: 18025032]

55. Hunder GG, Bloch DA, Michel BA et al.: The American College of Rheumatology 1990 criteria for the classification of giant cell arteritis. *Arthritis Rheum* 33: 1122, 1990.
[PubMed: 2202311]

56. Sanderson JC, Devine EB, Lipton RB et al.: Headache-related health resource utilisation in chronic and episodic migraine across six countries. *J Neurol Neurosurg Psychiatry* 84: 1309, 2013.
[PubMed: 23813744]

57. Valade D: Chronic migraine. *Rev Neurol (Paris)* 169: 419, 2013.
[PubMed: 23602118]

58. Mansfield LE: The role of antihistamine therapy in vascular headaches. *J Allergy Clin Immunol* 86: 673, 1990.
[PubMed: 2229834]

59. Kelley NE, Tepper DE: Rescue therapy for acute migraine, part 2: neuroleptics, antihistamines, and others. *Headache* 52: 292, 2012.
[PubMed: 22309235]

60. Kelley NE, Tepper DE: Rescue therapy for acute migraine, part 3: opioids, NSAIDs, steroids, and post-discharge medications. *Headache* 52: 467, 2012.
[PubMed: 22404708]

61. Rapoport AM, Tepper SJ, Bigal ME, Sheftell FD: The triptan formulations: how to match patients and products. *CNS Drugs* 17: 431, 2003.
[PubMed: 12697002]

62. Engindeniz Z, Demircan C, Karli N et al.: Intramuscular tramadol vs. diclofenac sodium for the treatment of acute migraine attacks in emergency department: a prospective, randomised, double-blind study. *J Headache Pain* 6: 143, 2005.
[PubMed: 16355295]

63. Worthington I, Pringsheim T, Gawel MJ et al.: Canadian Headache Society guideline: acute drug therapy for migraine headache. *Can J Neurol Sci* 40 (5 Suppl 3): S1, 2013.
[PubMed: 23968886]

64. Gilmore B, Michael M: Treatment of acute migraine headache. *Am Fam Physician* 83: 271, 2011.
[PubMed: 21302868]

65. Wall M, Kupersmith MJ, Kieburtz KD et al.: The idiopathic intracranial hypertension treatment trial: clinical profile at baseline. *JAMA Neurol* 71: 693, 2014.
[PubMed: 24756302]

66. Friedman DI, Liu GT, Digre KB: Revised diagnostic criteria for the pseudotumor cerebri syndrome in adults and children. *Neurology* 81: 1159, 2013.
[PubMed: 23966248]

67. Fiorito-Torres F, Rayhill M, Perloff M: Idiopathic intracerebral hypertension (IIH)/pseudotumor: removing less CSF is best (I9-1.006). *Neurology* 82 (10 Suppl): I9-1.006, 2014.

68. Friedman DI, Jacobson DM: Idiopathic intracranial hypertension. *J Neuroophthalmol* 24: 138, 2004.
[PubMed: 15179068]

69. Friedman DI: The pseudotumor cerebri syndrome. *Neurol Clin* 32: 363, 2014.
[PubMed: 24703535]

70. Arendt K, Demaerschalk BM, Wingerchuk DM, Camann W: Atraumatic lumbar puncture needles: after all these years, are we still missing the point? *Neurologist* 15: 17, 2009.
[PubMed: 19131853]

71. Frank LR, Paxson A, Brake J: Spontaneous intracranial hypotension—a case report. *J Emerg Med* 28: 427, 2005.
[PubMed: 15837024]

72. Liao YJ, Dillon WP, Chin CT, McDermott MW, Horton JC: Intracranial hypotension caused by leakage of cerebrospinal fluid from the thecal sac after lumboperitoneal shunt placement. Case report. *J Neurosurg* 107: 173, 2007.
[PubMed: 17639890]

73. Spears RC: Low-pressure/spinal fluid leak headache. *Curr Pain Headache Rep* 18: 425, 2014.
[PubMed: 24760494]

74. Basurto Ona X, Uriona Tuma SM, Martinez Garcia L, Sola I, Bonfill Cosp X: Drug therapy for preventing post-dural puncture headache. *Cochrane Database Syst Rev* 2: CD001792, 2013.
[PubMed: 23450533]

75. Van Horn A, Chamberlain MC: Neoplastic meningitis. *J Support Oncol* 10: 45, 2012.
[PubMed: 22005214]

76. Nesbitt AD, Goadsby PJ: Cluster headache. *BMJ* 344: e2407, 2012.
[PubMed: 22496300]

77. Petersen AS, Barloese MC, Jensen RH: Oxygen treatment of cluster headache: a review. *Cephalalgia* April 10, 2014. [Epub ahead of print]

78. Lagman-Bartolome AM: Metabolic headaches. *Neurol Clin* 32: 451, 2014.
[PubMed: 24703539]

79. Hu CM, Lin YJ, Fan YK, Chen SP, Lai TH: Isolated thunderclap headache during sex: Orgasmic headache or reversible cerebral vasoconstriction syndrome? *J Clin Neurosci* 17: 1349, 2010.
[PubMed: 20655230]

80. Cordenier A, De Hertogh W, De Keyser J, Versijpt J: Headache associated with cough: a review. *J Headache Pain* 14: 42, 2013.
[PubMed: 23687906]

81. Nawar RN, AbdelMannan D, Selman WR, Arafah BM: Pituitary tumor apoplexy: a review. *J Intensive Care Med* 23: 75, 2008.
[PubMed: 18372348]

82. Humphries RL, Stone CK, Bowers RC: Colloid cyst: a case report and literature review of a rare but deadly condition. *J Emerg Med* 40: e5, 2011.
[PubMed: 18814994]

83. Spears RC: Colloid cyst headache. *Curr Pain Headache Rep* 8: 297, 2004.
[PubMed: 15228889]

84. Chow AW, Benninger MS, Brook I et al.: IDSA clinical practice guideline for acute bacterial rhinosinusitis in children and adults. *Clin Infect Dis* 54: e72, 2012.
[PubMed: 22438350]