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perforation of abdominal viscera. A diagnosis of anemia may be more helpful than the white blood cell count, especially when combined with the history. The urinalysis may reveal the state of hydration or rule out severe renal disease, diabetes, or urinary infection. Blood urea nitrogen, glucose, and serum bilirubin levels and liver function tests may be helpful. Serum amylase levels may be increased by many diseases other than pancreatitis, for example, perforated ulcer, strangulating intestinal obstruction, and acute cholecystitis; thus, elevations of serum amylase do not rule in or rule out the need for an operation. Plain and upright or lateral decubitus radiographs of the abdomen have limited utility and may be unnecessary in some patients who have substantial evidence of some diseases such as acute appendicitis or strangulated external hernia. Where the indications for surgical or medical intervention are not clear, low-dose computed tomography is preferred to abdominal radiography when evaluating nontraumatic acute abdominal pain. Very rarely, barium or water-soluble contrast study of the upper part of the gastrointestinal tract is an appropriate radiographic investigation and may demonstrate partial intestinal obstruction that may elude diagnosis by other means. If there is any question of obstruction of the colon, oral administration of barium sulfate should be avoided. On the other hand, in cases of suspected colonic obstruction (without perforation), a contrast enema may be diagnostic. In the absence of trauma, peritoneal lavage has been replaced as a diagnostic tool by CT scanning and laparoscopy. Ultrasonography has proved to be useful in detecting an enlarged gallbladder or pancreas, the presence of gallstones, an enlarged ovary, or a tubal pregnancy. Laparoscopy is especially helpful in diagnosing pelvic conditions, such as ovarian cysts, tubal pregnancies, salpingitis, acute appendicitis, and other disease processes. Laparoscopy has a particular advantage over imaging in that the underlying etiologic condition can often be definitively addressed. Radioisotopic hepatobiliary iminodiacetic acid scans (HIDAs) may help differentiate acute cholecystitis or biliary colic from acute pancreatitis. A CT scan may demonstrate an enlarged pancreas, ruptured spleen, or thickened colonic or appendiceal wall and streaking of the mesocolon or mesoappendix characteristic of diverticulitis or appendicitis. Sometimes, even under the best circumstances with all available aids and with the greatest of clinical skill, a definitive diagnosis cannot be established at the time of the initial examination. And, in some cases, operation may be indicated based on clinical grounds alone. Should that decision be questionable, watchful waiting with repeated questioning and examination will often elucidate the true nature of the illness and indicate the proper course of action. Acknowledgment The author gratefully acknowledges the enormous contribution to this chapter and the approach it espouses to William Silen, who authored this chapter for many previous editions. ■ ■ FURTHER READING Bhangu A et al: Acute appendicitis: Modern understanding of pathogenesis, diagnosis and management. *Lancet* 386:1278, 2015. Cartwright SL, Knudson MP: Diagnostic imaging of acute abdominal pain in adults. *Am Fam Phys* 91:452, 2015. Huckins DS et al: Diagnostic performance of a biomarker panel as a

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Headache Headache is among the most common reasons patients seek medical attention and is responsible, on a global basis, for more disability than any other neurologic problem. Diagnosis and management are based on a careful clinical approach augmented by an understanding of the anatomy, physiology, and pharmacology of the nervous system pathways mediating the various headache syndromes. This chapter will focus on the general approach to a patient with headache; migraine and other primary headache disorders are discussed in Chap. 441. Headache CHAPTER 17

■ ■GENERAL PRINCIPLES A classification system developed by the International Headache Society (www.ihs-headache.org/en/resources/guidelines/) characterizes headache disorders as primary or secondary (Table 17-1). Primary headaches are those in which headache and its associated features form the disorder itself, whereas secondary headaches are those caused by exogenous disorders (Headache Classification Committee of the International Headache Society, 2018).

Primary headache often results in considerable disability and a decrease in the patient's quality of life. Mild secondary headache, such as that seen in association with upper respiratory tract infections, is common but rarely worrisome. Lifethreatening headache is relatively uncommon, with vigilance required to recognize and appropriately treat such patients. ■ ■ANATOMY AND

PHYSIOLOGY OF HEADACHE Pain usually occurs when peripheral nociceptors are stimulated in response to tissue injury, visceral distension, or other factors (Chap. 14). In such situations, pain perception is a normal physiologic response mediated by a healthy nervous system. Pain can also result when painproducing pathways of the peripheral or central nervous system (CNS) are damaged or activated inappropriately. Headache may originate from either or both mechanisms. Relatively few cranial structures are pain-producing; these include the scalp, meningeal arteries, dural sinuses, falx cerebri, and proximal segments of the large pial arteries. The ventricular ependyma, choroid plexus, pial veins, and much of the brain parenchyma are not pain-producing. The key structures involved in primary headache appear to be: • The large intracranial vessels and dura mater and the peripheral terminals of the trigeminal nerve that innervate these structures •

The caudal portion of the trigeminal nucleus, which extends into the dorsal horns of the upper cervical spinal cord and receives input from the first and second cervical nerve roots (the trigeminocervical complex) • Rostral pain-processing regions, such as the ventroposteromedial thalamus and the cortex • The pain-modulatory systems in the brain that modulate input from trigeminal nociceptors at all levels of the pain-processing pathways and influence vegetative functions, such as hypothalamus and brain stem structures TABLE 17-1 Common Causes of

Headache PRIMARY HEADACHE SECONDARY HEADACHE TYPE % TYPE % Tension-type

Systemic infection

Migraine

Head injury

Idiopathic stabbing

Vascular disorders

Exertional

Subarachnoid hemorrhage <1 Cluster 0.1 Brain tumor 0.1 Source: After J Olesen et al: The Headaches. Philadelphia, Lippincott Williams & Wilkins, 2005.

The innervation of the large intracranial vessels and dura mater by the trigeminal nerve is known as the trigeminovascular system. Cranial autonomic symptoms, such as lacrimation, conjunctival injection, nasal congestion, rhinorrhea, periorbital swelling, aural fullness, and ptosis, are prominent in the trigeminal autonomic cephalalgias (TACs), including cluster headache and paroxysmal hemicrania, and are often seen in migraine, even in children. These cranial autonomic symptoms reflect activation of cranial parasympathetic pathways, and functional imaging studies indicate that vascular changes in migraine and cluster headache, when present, are similarly driven by these cranial autonomic systems. Thus, they are secondary, and not causative, events in the headache cascade. Moreover, they can often be mistaken for symptoms or signs of cranial sinus inflammation, which is then overdiagnosed and inappropriately managed. Migraine and other primary headache disorders are not “vascular headaches”; these disorders do not reliably manifest vascular changes, and treatment outcomes cannot be predicted by vascular effects. Migraine is a brain disorder and is best understood and managed as such.

PART 2 Cardinal Manifestations and Presentation of Diseases ■ ■CLINICAL EVALUATION OF ACUTE,

NEW-ONSET HEADACHE The patient who presents with a new, severe headache has a differential diagnosis that is quite different from the patient with recurrent headaches over many years. In new-onset and severe headache, the probability of finding a potentially serious cause is considerably greater than in recurrent headache. Patients with recent onset of pain require prompt evaluation and appropriate treatment. Serious causes to be considered include meningitis, subarachnoid hemorrhage, epidural or subdural hematoma, glaucoma, tumor, and purulent sinusitis. When worrisome symptoms and signs are present (Table 17-2), rapid diagnosis and management are critical. A careful neurologic examination is an essential part of the first step evaluation. In most cases, patients with an abnormal examination, or a history of recent-onset headache, should be evaluated by a computed tomography (CT) or magnetic resonance imaging (MRI) study of the brain. As an initial screening procedure for intracranial pathology in this setting, CT and MRI methods appear to be equally sensitive. In some circumstances, a lumbar puncture (LP) is also required, unless a benign etiology can be otherwise established. A general evaluation of acute headache might include cranial arteries by palpation; cervical spine by the effect of passive movement of the head and by imaging; the investigation of cardiovascular and renal status by blood pressure monitoring and urine examination; and eyes by funduscopy, intraocular pressure measurement, and refraction. The psychological state of the patient should also be evaluated because a relationship exists between head pain, depression, and anxiety. This is intended to identify comorbidity rather than provide an explanation for the headache, because troublesome headache is seldom simply caused by mood change. Although it is notable that some medicines with antidepressant actions are also effective in the preventive

TABLE 17-2 Headache Symptoms

That Suggest a Serious Underlying Disorder Sudden-onset headache First severe headache Vomiting that precedes headache Subacute worsening over days or weeks Pain induced by bending, lifting, cough Pain that disturbs sleep or presents immediately upon awakening Known systemic illness "Worst" headache ever Onset after age 55 Fever or unexplained systemic signs Abnormal neurologic examination Pain associated with local tenderness, e.g., region of temporal artery

treatment of both tension-type headache and migraine, each symptom must be treated optimally. Underlying recurrent headache disorders may be activated by pain that follows otologic or endodontic surgical procedures. Thus, pain about the head as the result of diseased tissue or trauma may reawaken an otherwise quiescent migraine syndrome. Treatment of the head ache is largely ineffective until the cause of the primary problem is addressed. Serious underlying conditions that are associated with headache are described below. Brain tumor is a rare cause of isolated headache and even less commonly a cause of severe pain. The vast majority of patients presenting with severe headache have a benign cause, usually migraine. **SECONDARY HEADACHE** The management of secondary headache focuses on diagnosis and treatment of the underlying condition. ■ ■ **MENINGITIS** Acute, severe headache with stiff neck and fever suggests meningitis. LP is mandatory. Often there is striking accentuation of pain with eye movement. Meningitis can be easily mistaken for migraine in that the cardinal symptoms of pounding headache, photophobia, nausea, and vomiting are frequently present, perhaps reflecting the underlying biology of some of the patients. Meningitis is discussed in Chaps. 143 and 144. ■ ■ **INTRACRANIAL HEMORRHAGE** Acute, maximal in <5 min, severe headache lasting >5 min with stiff neck but without fever suggests subarachnoid hemorrhage. A ruptured aneurysm, arteriovenous malformation, or intraparenchymal hemorrhage may also present with headache alone. Rarely, if the hemorrhage is small or below the foramen magnum, the head CT scan can be normal. Therefore, LP may be required to diagnose definitively sub arachnoid hemorrhage. Subarachnoid hemorrhage is discussed in Chap. 440, and intra cranial hemorrhage in Chap. 439. ■ ■ **BRAIN TUMOR** Approximately 30% of patients with brain tumors consider headache to be their chief complaint. The head pain is usually nondescript—an intermittent deep, dull aching of moderate intensity, which may worsen with exertion or change in position and may be associated with nausea and vomiting. This pattern of symptoms results from migraine far more often than brain tumor. The headache of brain tumor disturbs sleep in about 10% of patients. Vomiting that precedes the appearance of headache by weeks is highly characteristic of posterior fossa brain tumors. A history of amenorrhea or galactorrhea with headache suggests a possible prolactin-secreting pituitary adenoma or the polycystic ovary syndrome. Headache arising de novo in a patient with known malignancy suggests either cerebral metastases or carcinomatous meningitis. Head pain appearing abruptly after bending, lifting, or coughing can be due to a posterior fossa mass, a Chiari malformation, or low cerebrospinal fluid (CSF) volume. Brain tumors are discussed in Chap. 95. ■ ■ **TEMPORAL ARTERITIS** (See also Chaps. 34 and 375) Temporal (giant cell) arteritis is an inflammatory disorder of arteries that frequently involves the extra cranial carotid circulation. It is a common disorder of the elderly; its annual incidence is 77 per 100,000 individuals aged ≥50. The average age of onset is 70 years, and women account for 65% of cases. About half of patients with untreated temporal arteritis develop blindness due to involvement of the ophthalmic artery and its branches; indeed, ischemic optic neuropathy induced by giant cell arteritis is the major cause of rapidly developing bilateral blindness in patients >60 years. Because treatment with glucocorticoids is effective in preventing this complication, prompt recognition of the disorder is

important. Typical presenting symptoms include headache, polymyalgia rheumatica (Chap. 375), jaw claudication, fever, and weight loss. Headache

is the dominant symptom and often appears in association with malaise and muscle aches. Head pain may be unilateral or bilateral and is located temporally in 50% of patients but may involve any and all aspects of the cranium. Pain usually appears gradually over a few hours before peak intensity is reached; occasionally, it is explosive in onset. The quality of pain is infrequently throbbing; it is almost invariably described as dull and boring, with superimposed episodic stabbing pains similar to the sharp pains that appear in migraine. Most patients can recognize that the origin of their head pain is superficial, external to the skull, rather than originating deep within the cranium (the pain site usually identified by migraineurs). Scalp tenderness is present, often to a marked degree; brushing the hair or resting the head on a pillow may be impossible because of pain. Headache is usually worse at night and often aggravated by exposure to cold. Additional findings may include reddened, tender nodules or red streaking of the skin overlying the temporal arteries, and tenderness of the temporal or, less commonly, the occipital arteries. The erythrocyte sedimentation rate (ESR) is often, although not always, elevated; a normal ESR does not exclude giant cell arteritis. A temporal artery biopsy followed by immediate treatment with prednisone 80 mg daily for the first 4–6 weeks should be initiated when clinical suspicion is high. The prevalence of migraine among the elderly is substantial, considerably higher than that of giant cell arteritis. Migraineurs often report amelioration of their headaches with prednisone; thus, caution must be used when interpreting the therapeutic response. ■ ■GLAUCOMA Glaucoma may present with a prostrating headache associated with nausea and vomiting. The headache often starts with severe eye pain. On physical examination, the eye is often red with a fixed, moderately dilated pupil. Glaucoma is discussed in Chap. 34. PRIMARY HEADACHE DISORDERS Primary headaches disorders generally manifest as headache and associated features occurring in the absence of any exogenous cause. The most common are migraine, tension-type headache, and the trigeminal autonomic cephalalgias (TACs), notably cluster headache. These entities are discussed in detail in Chap. 441. ■ ■CHRONIC DAILY OR NEAR-DAILY HEADACHE The broad description of chronic daily headache (CDH) can be applied when a patient experiences headache on 15 days or more per month. CDH is not a single entity, nor a diagnosis; it encompasses a number of different headache syndromes, both primary and secondary (Table 17-3). TABLE 17-3 Classification of Daily or Near-Daily Headache Primary

“ 4 H DAILY <4 H DAILY SECONDARY Chronic migraine Chronic cluster headache Posttraumatic Head injury Iatrogenic Postinfectious Chronic tension-type headache Chronic paroxysmal hemicrania Inflammatory, such as Giant cell arteritis Sarcoidosis Behçet’s syndrome Hemicrania continua SUNCT/SUNA Chronic CNS infection New daily persistent headache Hypnic headache Medication-overuse headache aMay be complicated by medication overuse. bSome patients may have headache 4 h/d. Abbreviations: CNS, central nervous system; SUNA, short-lasting unilateral neuralgiform headache attacks with cranial autonomic symptoms; SUNCT, shortlasting unilateral neuralgiform headache attacks with conjunctival injection and tearing.

In aggregate, this group presents considerable disability and is thus specifically mentioned here. Population-based estimates suggest that about 4% of adults have daily or near-daily headache.

APPROACH TO THE PATIENT Chronic Daily Headache The first step in the management of patients with CDH is to diagnose any secondary headache and treat that problem (Table 17-3). This can sometimes be a challenge when the underlying cause triggers worsening of a primary headache. For patients with primary headache disorders, diagnosis of the headache type will guide therapy. Preventive treatments such as tricyclics, either amitriptyline or nortriptyline at doses up to 1 mg/kg, are very useful in patients with CDH arising from migraine or tension-type headache or where the secondary cause has activated the underlying primary headache. Tricyclics are started in low doses (10–25 mg) daily and may be given 12 h before the expected time of awakening in order to avoid excessive morning sleepiness. Medicines including topiramate, valproate, propranolol, flunarizine (not available in the United States), candesartan, and the newer calcitonin gene-related peptide (CGRP) pathway monoclonal antibodies and CGRP receptor antagonists (gepants; see Chap. 441) are also useful when the underlying issue is migraine. Headache

CHAPTER 17 MANAGEMENT OF MEDICALLY INTRACTABLE DISABLING PRIMARY HEADACHE The management of medically intractable headache is difficult, although recent developments in therapy have proved effective. Monoclonal antibodies to CGRP or its receptor, or CGRP receptor antagonists (gepants), are effective and well-tolerated in chronic migraine and licensed for use in clinical practice. Noninvasive neuromodulatory approaches, such as single-pulse transcranial magnetic stimulation and remote electrical neuromodulation, which appear to modulate thalamic processing or brainstem mechanisms, respectively, in migraine have been used in clinical practice with success (Chap. 441). Noninvasive vagal nerve stimulation has also shown promise, particularly in cluster headache, chronic paroxysmal hemicrania, and hemicrania continua, and possibly in short-lasting unilateral neuralgiform headache attacks with cranial autonomic symptoms (SUNA) and short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing (SUNCT) (Chap. 441). Other modalities are discussed in Chap. 441. **MEDICATION-RELATED AND MEDICATION-OVERUSE HEADACHE** Overuse of analgesic medication for headache can aggravate headache frequency, markedly impair the effect of preventive medicines, and induce a state of refractory daily or near-daily headache called medication-overuse headache. A proportion of patients who stop taking analgesics will experience substantial improvement in the severity and frequency of their headache. However, even after cessation of analgesic use, many patients continue to have headache, although they may feel clinically improved in some way, especially if they have been using opioids or barbiturates regularly. The residual symptoms probably represent the underlying primary headache disorder, and most commonly, this issue occurs in patients prone to migraine. **Management of Medication Overuse: Outpatients** For patients who overuse analgesic medications, it is often helpful to reduce and eliminate them, although this strategy is far from universally effective. One approach is to reduce the medication dose by 10% every 1–2 weeks. Immediate cessation of analgesic use is possible for some patients, provided there is no contraindication. Both approaches are facilitated by use of a medication diary maintained during the month or two before cessation; this helps to identify the scope of the problem. A small dose of a nonsteroidal anti-

inflammatory drug (NSAID) such as naproxen, 500 mg bid, if tolerated, will help relieve residual pain as analgesic use is reduced.

NSAID overuse is not usually a problem for patients with daily headache when a NSAID with a longer half-life is taken once or twice daily. Once the patient has substantially reduced analgesic use, a preventive medication should be introduced. Another widely used approach is to commence the preventive at the same time the analgesic reduction is started; both approaches are supported by controlled trial data. A common cause of unresponsiveness to treatment is the use of a preventive when analgesics continue to be used regularly. For some patients, discontinuing analgesics is very difficult; often the best approach is to inform the patient that some degree of pain is inevitable during this initial period.

PART 2 Cardinal Manifestations and Presentation of Diseases Management of Medication Overuse or Treatment-Refractory Headache: Inpatients Some patients will require hospitalization for detoxification and management. Such patients have typically failed efforts at outpatient withdrawal or have a significant medical condition, such as diabetes mellitus or epilepsy, that would complicate withdrawal as an outpatient. Following admission to the hospital, medications are withdrawn completely on the first day, in the absence of a contraindication. Antiemetics and fluids are administered as required; clonidine is used for opioid withdrawal symptoms. For acute intolerable pain during the waking hours, aspirin, 1 g IV (not approved in United States), is useful. IM chlorpromazine can be helpful at night; patients must be adequately hydrated. Three to five days into the admission, as the effect of the withdrawn substance wears off, a course of IV dihydroergotamine (DHE) can be used. DHE, administered every 8 h for 5 consecutive days, a treatment that is not stopped short if headache settles, can induce a significant remission that allows a preventive treatment to be established. Serotonin 5-HT₃ receptor antagonists, such as ondansetron or granisetron, or the neurokinin receptor antagonist aprepitant may be required with DHE to prevent significant nausea, and domperidone (not approved in the United States) orally or by suppository can be very helpful. Avoiding sedating or otherwise side effect-prone antiemetics is helpful. Alternatives include a 7- to 10-day course of IV lidocaine or IV divalproex sodium or use of the CGRP antagonist eptinezumab intravenously (Table 441-6).

NEW DAILY PERSISTENT HEADACHE New daily persistent headache (NDPH) is a clinically distinct syndrome with important secondary causes; these are listed in Table 17-4.

Clinical Presentation NDPH presents with headache on most if not all days, and the patient can clearly, and often vividly, recall the moment of onset. The headache usually begins abruptly, but onset may be more gradual; evolution over 3 days has been proposed as the upper limit for this syndrome. Patients typically recall the exact day and circumstances of the onset of headache; the new, persistent head pain does not remit. The first priority is to distinguish between a primary and a secondary cause of this syndrome. Subarachnoid hemorrhage is the most serious of the secondary causes and must be excluded either by history or appropriate investigation (Chap. 440).

Secondary NDPH • Low CSF Volume Headache In these syndromes, head pain is positional: it begins when the patient sits

TABLE 17-4 Differential Diagnosis of New Daily Persistent Headache	
PRIMARY	Migrainous-type
SECONDARY	Subarachnoid hemorrhage
	Featureless (tension-type)
	Low cerebrospinal fluid (CSF) volume headache
	Raised CSF pressure headache
	Posttraumatic headache
	Chronic meningitis

Includes postinfectious forms.

or stands upright and resolves upon reclining. The pain, which is occipitofrontal, is usually a dull ache but may be throbbing. Patients with chronic low CSF volume headache typically present with a history of headache from one day to the next that is generally not present on waking but worsens during the day. Recumbency usually improves the headache within minutes, and it can take only minutes to an hour for the pain to return when the patient resumes an upright position. The most common cause of headache due to persistent low CSF volume is CSF leak following LP (Chap. 53).

Post-LP headache usually begins within 48 h but may be delayed for up to 12 days. Its incidence is between 10 and 30%. Beverages with caffeine may provide temporary relief. Besides LP, index events may include epidural injection or a vigorous Valsalva maneuver, such as from lifting, straining, coughing, clearing the eustachian tubes in an airplane, or multiple orgasms. Spontaneous CSF leaks are well recognized, and the diagnosis should be considered whenever the headache history is typical, even when there is no obvious index event. As time passes from the index event, the postural nature may become less apparent; cases in which the index event occurred several years before the eventual diagnosis have been recognized. Symptoms appear to result from low volume rather than low pressure: although low CSF pressures, typically 0–50 mm CSF, are usually identified, a pressure as high as 140 mm CSF has been noted with a documented leak. Postural orthostatic tachycardia syndrome (POTS; Chap. 451) can present with orthostatic headache similar to low CSF volume headache and is a diagnosis that needs consideration in this setting. When imaging is indicated to identify the source of a presumed leak, an MRI with gadolinium is the initial study of choice (Fig. 17-1). A striking pattern of diffuse meningeal enhancement is so typical that in the appropriate clinical context the diagnosis is established. Chiari malformations may sometimes be noted on MRI; in such cases, surgery to decompress the posterior fossa is not indicated and usually worsens the headache. Spinal MRI with T2 weighting may reveal a leak, and spinal MRI may demonstrate spinal meningeal cysts whose role in these syndromes is yet to be elucidated. The source of CSF leakage may be identified by spinal MRI with appropriate sequences, or by CT, preferably lateral decubitus digital subtraction, myelography. In the absence of a directly identified site of leakage, ¹¹¹In-DTPA CSF studies may demonstrate early emptying of the tracer into the bladder or slow progress of tracer across POST CONTRAST POST CONTRAST FIGURE 17-1 Magnetic resonance image showing diffuse meningeal enhancement after gadolinium administration in a patient with low cerebrospinal fluid (CSF) volume headache.

the brain suggesting a CSF leak; this procedure is now only rarely employed. Initial treatment for low CSF volume headache is bed rest. For patients with persistent pain, IV caffeine (500 mg in 500 mL of saline administered over 2 h) can be very effective. An electrocardiogram (ECG) to screen for arrhythmia should be performed before administration. It is reasonable to administer at least two infusions of caffeine before embarking on additional tests to identify the source of the CSF leak. Because IV caffeine is safe and can be curative, it spares many patients the need for further investigations. If unsuccessful, an abdominal binder may be helpful. If a leak can be identified, an autologous blood patch is usually curative. A blood patch is also effective for post-LP headache; in this setting, the location is empirically determined to be the site of the LP. In patients with intractable headache, oral theophylline is a useful alternative that can take some months to be effective. CSF-venous fistulas require closure. Raised CSF Pressure Headache Raised CSF pressure is well recognized as a cause of headache. Brain imaging can often reveal the cause, such as a space-occupying lesion. Idiopathic Intracranial Hypertension (Pseudotumor Cerebri) NDPH due to raised CSF pressure can be the presenting symptom for patients with idiopathic intracranial hypertension, a disorder associated with obesity, female gender, and, on occasion, pregnancy. The syndrome can also occur without visual problems, particularly when the fundi are normal. These patients typically present with a history of generalized headache that is present on awakening, improves as the day goes on, and worsens with recumbency. Transient visual obscurations are frequent and may occur when the headaches are most severe. The diagnosis is relatively straightforward when papilledema is present, but the possibility must be considered even in patients without funduscopic changes. Formal visual field testing should be performed even in the absence

of overt ophthalmic involvement. Partial obstructions of the cerebral venous sinuses are found in a small number of cases. In addition, persistently raised intracranial pressure can trigger a syndrome of chronic migraine. Other conditions that characteristically produce headache on rising in the morning or nocturnal headache are obstructive sleep apnea or poorly controlled hypertension. Evaluation of patients suspected to have raised CSF pressure requires brain imaging. It is most efficient to obtain an MRI, including an MR venogram, as the initial study. If there are no contraindications, the CSF pressure should be measured by LP; this should be done when the patient is symptomatic so that both the pressure and the response to removal of 20–30 mL of CSF can be determined. An elevated opening pressure and improvement in headache following removal of CSF are diagnostic in the absence of fundal changes. Initial treatment is with acetazolamide (250–500 mg bid); the headache may improve within weeks. A plan for weight loss should also be instituted when required. If ineffective, topiramate is the next treatment of choice; it has many actions that may be useful in this setting, including carbonic anhydrase inhibition, weight loss, and neuronal membrane stabilization, likely mediated via effects on phosphorylation pathways. Severely disabled patients who do not respond to medical treatment require intracranial pressure monitoring and may require shunting.

Posttraumatic Headache A traumatic event can trigger a headache process that lasts for many months or years after the event. The term trauma is used here in a very broad sense: headache can develop following an injury to the head, but it can also develop after an infectious episode, typically viral meningitis, a flulike illness (see below), or a parasitic infection. Complaints of dizziness, vertigo, and impaired memory can accompany the headache. Symptoms may remit after several weeks or persist for months and even years

after the injury. Typically, the neurologic examination is normal and CT or MRI studies are unrevealing. Chronic subdural hematoma may on occasion mimic this disorder. Posttraumatic headache may also be seen after carotid dissection and subarachnoid hemorrhage and after intracranial surgery. The underlying theme appears to be that a traumatic event involving the pain-producing meninges can trigger a headache process that lasts for many years.

Other Causes In one series, one-third of patients with NDPH reported headache beginning after a transient flulike illness characterized by fever, neck stiffness, photophobia, and marked malaise. Evaluation typically reveals no apparent cause for the headache. There is no convincing evidence that persistent Epstein-Barr virus infection plays a role in NDPH. A complicating factor is that many patients undergo LP during the acute illness; iatrogenic low CSF volume headache must be considered in these cases. Post-COVID-19 onset of NDPH is now well documented.

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Treatment Treatment is largely empirical and directed at the headache phenotype. Tricyclic antidepressants, notably amitriptyline, and anticonvulsants, such as topiramate, valproate, candesartan, and gabapentin, have been used with reported benefit, as have CGRP pathway blockers (monoclonal antibodies and gepants). The monoamine oxidase inhibitor phenelzine may also be useful in carefully selected patients. The headache usually resolves within 3–5 years, but it can be quite disabling.

PRIMARY CARE AND HEADACHE MANAGEMENT Most patients with headache will be seen first in a primary care setting. The challenging task of the primary care physician is to identify the very few worrisome secondary headaches from the very great majority of primary and less dangerous secondary headaches (Table 17-2). Absent any warning signs, a reasonable approach is to treat when a diagnosis is established. As a general rule, the investigation should focus on identifying worrisome causes of headache or on helping the patient to gain confidence if no primary headache diagnosis can be made. After treatment has been initiated, follow-up care is essential to identify whether progress has been made against the headache complaint. Not all headaches will respond to treatment, but, in general, worrisome headaches will progress and will

be easier to identify. When a primary care physician feels the diagnosis is a primary headache disorder, it is worth noting that >90% of patients who present to primary care with a complaint of headache will have migraine (Chap. 441). In general, patients who do not have a clear diagnosis, have a primary headache disorder other than migraine or tension-type headache, or are unresponsive to two or more standard therapies for the considered headache type should be referred to a specialist. In a practical sense, the threshold for referral is also determined by the experience of the primary care physician in headache medicine and the availability of secondary care options. ■ ■FURTHER READING Headache Classification Committee of the International Headache Society: The International Classification of Headache Disorders, 3rd ed. Cephalalgia 38:1, 2018. Kernick D, Goadsby PJ: Headache: A Practical Manual, 2nd ed. Oxford, Oxford University Press, 2024. Lance JW, Goadsby PJ: Mechanism and Management of Headache, 7th ed. New York, Elsevier, 2005. Olesen J et al: The Headaches. Philadelphia, Lippincott, Williams & Wilkins, 2005. Silberstein SD et al: Wolff's Headache and Other Head Pain, 9th ed. New York, Oxford University Press, 2021.

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