

# Pitfalls in the Management of Headache in the Emergency Department

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## KEYWORDS

• Headache • Cephalgia • Emergency medicine

Headache, or cephalgia, is the fifth most common primary complaint of patients presenting to an emergency department (ED) in the United States, representing more than 3 million patients each year, or 2% of all ED visits.<sup>1</sup> An additional number seek treatment at ambulatory care clinics, where diagnostic capabilities may be more limited. When headache coexists with certain other presenting signs and symptoms, such as alteration of mental status or hypoxia, these features may overshadow the headache and will likely direct the diagnostic and therapeutic approach. This article focuses on patients for whom headache is their most prominent presenting complaint.

The role of the emergency physician (EP) is unique in the evaluation and treatment of headache, one that differs from that of the primary care physician, the neurologist, and other specialists. The EP has 2 major responsibilities: to relieve headache pain and to ensure that life-threatening and disabling underlying causes are uncovered and treated. As with other cardinal presentations, these 2 priorities are addressed simultaneously. Because most patients with headache are subsequently discharged home, appropriate follow-up planning and patient education are also important aspects of emergency care. The pitfalls that follow are those most frequently encountered in emergency medicine practice and those with the greatest likelihood to adversely affect patient outcomes.

## PITFALLS OF NOMENCLATURE

### *Being Too Specific*

The underlying pathophysiologic mechanisms of many types of headache are still poorly defined, and diagnostic terminology is rapidly evolving. The International

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Headache Society, a multidisciplinary group of clinicians and scholars, has attempted to provide a standard nomenclature to aid in the study and treatment of the various disorders that result in headache. The most recent edition of their classification scheme, the International Classification of Headache Disorders (ICHD-2), provides an exhaustive, categorized list of more than 200 disease entities, each with specific, detailed diagnostic criteria.<sup>2</sup> However, from an emergency medicine perspective, such diagnostic precision is unnecessary, and may distract the clinician from important priorities in the ED.

At the most basic level, most investigators, including those of the ICHD-2, classify headaches as primary or secondary. Primary headaches are those that cannot be attributed to another known disease or condition, and include migraine, tension, and cluster headaches. Because their underlying causes are still being elucidated, they are classified according to their symptomatology. Secondary headaches are classified according to their underlying cause. All of the specific diagnoses that require time-dependent therapies in the ED to prevent poor patient outcomes are of secondary headaches.

Several investigators have brought attention to the lack of diagnostic accuracy applied to patients with primary headache in the ED, most notably for those with migraine.<sup>3-5</sup> They propose that increasing accuracy would allow for therapy that is more targeted and appropriate to specific underlying diagnoses. However, there is remarkable overlap in the response of the various subclasses of primary headache to the different agents and regimens used to treat headache pain in the ED. In one recent study, a dedicated research assistant performed a detailed interview of ED patients with headache, and formally classified them into ICHD-2 categories.<sup>6</sup> No difference was found in their response to sumatriptan, an antimigraine therapy, regardless of whether they were classified as having migraine, probable migraine, or tension headache. Similarly, patients treated with antiemetics, opioids, and dihydroergotamine (DHE) show excellent response to therapy, regardless of their specific underlying diagnosis.<sup>7</sup> Moreover, it may be difficult to make a specific diagnosis in the ED; many of the diagnostic criteria involve the observation of headache patterns over time, and are best evaluated in the interval between acute episodes. In one study of ED patients, even when a structured questionnaire based on ICHD-2 was applied, no specific diagnosis could be made in more than one-third of cases.<sup>8</sup>

Although it may be appropriate to make specific diagnoses in individual cases, a premature diagnosis of migraine, or another subclass of primary headache, may have other adverse consequences. Such a diagnosis may inappropriately stigmatize the patient with a chronic medical condition. More importantly, such a diagnosis may result in anchoring bias, which is the tendency to ignore important data by relying too heavily on 1 trait or source of information, such as a previous diagnosis, when making decisions. Thus, it may prevent the clinician from pursuing further appropriate evaluation to reach another correct diagnosis of a secondary headache. In a recent study performed in a community ED, patients with a previous diagnosis of migraine headache did not meet widely accepted diagnostic criteria.<sup>9</sup> Unless all of the elements necessary for the diagnosis are present, it may be more prudent to leave definitive diagnosis to the primary care provider or specialist consultant.

### ***Dangerous Primary Headache Diagnoses***

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Some of the specific primary headache diagnoses listed in the ICHD-2 are fraught with hazard for the EP and the primary care physician. Entities such as hemiplegic migraine and thunderclap headache mimic life-threatening secondary headaches such as stroke and subarachnoid hemorrhage (SAH) in their clinical presentation. For this

reason, these are conditions that cannot be diagnosed without a thorough diagnostic evaluation and subsequent follow-up. It is inadvisable for the EP to make these diagnoses de novo without specialist consultation.

## **PITFALLS OF HISTORY AND PHYSICAL EXAMINATION**

### ***Linking Treatment Response to Diagnosis***

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One dangerous and common misunderstanding is that primary headaches may be differentiated from secondary headaches based on a patient's response to analgesic agents. Because headache pain seems to be mediated through a limited number of final common physiologic pathways, response to analgesia may provide few, if any, clues to the underlying cause. Life-threatening secondary headaches may resolve with antimigraine therapies, simple analgesics such as acetaminophen, or even spontaneously without treatment. A positive response to analgesics and antimigraine therapy has been reported with virtually every category of secondary headache, including carotid artery dissection, carbon monoxide (CO) exposure, brain tumor, SAH, meningitis, and venous sinus thrombosis (VST).<sup>10-17</sup>

### ***Dismissing Secondary Headache Diagnoses in Patients with Known Primary Headaches***

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A small number of patients with headache account for a disproportionately large number of ED visits.<sup>18,19</sup> Many of these patients carry established specific primary headache diagnoses, most commonly migraine.<sup>19</sup> As every EP knows, sometimes the biggest impediment to a new, correct diagnosis is a current longstanding diagnosis. In addition, a history of migraine headache may increase the risk for some life-threatening causes of secondary headaches, such as ischemic stroke.<sup>20</sup> Practitioners must be careful to consider each new headache presentation for features that may distinguish it from previous headaches and warrant further investigation.

### ***Ascribing Headaches to Increased Blood Pressure***

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It is common for patients to ascribe headache pain to elevated blood pressure. Although patients with hypertensive encephalopathy may suffer from headache in association with severely elevated blood pressure, this condition is rare and requires additional features for diagnosis, such as an alteration in mental status. In most cases, mild, moderate, and even severe elevations of blood pressure are likely unrelated to headaches and other acute symptomatology that is frequently ascribed to hypertension.<sup>21</sup> Conversely, acute pain syndromes, such as headache, may result in increases in blood pressure, and the treatment of pain should be the first approach in these patients. In the absence of acute end-organ injury, the aggressive treatment of increased blood pressure with antihypertensive agents may result in undesirable and precipitous drops in blood pressure that, in turn, may cause watershed ischemia and stroke in patients with longstanding hypertension.

### ***Historical Features of SAH***

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Of all of the causes of secondary headache, SAH is of foremost concern for the EP because it commonly presents as an isolated headache in the absence of other findings, and it is highly lethal if left undiagnosed. Generations of medical students have been taught to link "the worst headache of your life" with the diagnosis of nontraumatic SAH. Although some patients who describe their headache in this way are ultimately found to have SAH or other life-threatening secondary headache, most do not.<sup>22,23</sup> In addition, there seems to be an inherent inconsistency in how patients answer questions related to the intensity of their headache. In one recent study,

one-third of patients who stated that their headache was the worst of their life subsequently were able to identify a previous headache of equal intensity.<sup>24</sup> Using this single descriptor alone, without further delineation to direct a workup for secondary causes of headache, may lead to an ineffective use of resources and unnecessary complications of the various studies used.

It is more helpful to elicit descriptors that characterize the suddenness of headache onset, its intensity at onset, and how the headache compares in quality to any previous headaches. Patients who describe a headache that is sudden in onset and maximum in intensity immediately or within a few minutes of onset, the so-called thunderclap headache, are much more likely to harbor serious pathology. Two studies that prospectively examined patients with severe, sudden-onset headache found significant numbers (44% and 71%) with SAH or other serious pathologies.<sup>25,26</sup> This has led to the recommendation by the American College of Emergency Physicians that patients with thunderclap headache undergo emergent neuroimaging followed by cerebrospinal fluid (CSF) analysis if imaging studies do not reveal a diagnosis.<sup>27</sup>

The familiar descriptor of the “worst headache of your life” may also serve clinicians poorly when patients present with sudden-onset, maximal-at-onset headaches that are not necessarily perceived as severe. Studies of patients with confirmed SAH have consistently found that many had presented previously with a new symptom of headache in the days and weeks that preceded their diagnosis and admission to hospital. The initial headache is often dismissed as benign after it remits spontaneously or with analgesics.<sup>28</sup> In some cases, patients do not seek medical attention. This is consistent with the natural history of aneurysmal SAH, in which a small, symptomatic leak is typically followed by a more severe, disabling, and life-threatening bleed in the days and weeks that follow. Patients with aneurysmal SAH are served best if the diagnosis is made in this interval, when neurosurgical intervention can forestall disaster. Although the precise incidence of this phenomenon is difficult to ascertain, because of variable workups performed for sudden-onset headache in different clinical settings and recall bias on the part of survivors, studies have found rates of so-called sentinel leak ranging from 10% to 43%.<sup>29</sup> Thus, any headache that is sudden in onset, maximal at onset, and different in nature from headaches that the patient has had in the past deserves a diagnostic workup.

### ***Other Critical History and Physical Examination Features***

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As with any cardinal complaint, the EP considers all causes of headache that are life threatening or disabling and for which a critical intervention may be indicated. This list of secondary headaches is summarized in **Table 1**. Each diagnosis is associated with critical features on history and physical examination, and if these features are present, a diagnostic workup is indicated. Likewise, in most patients with a primary headache diagnosis, for whom diagnostic testing is not necessary, the absence of these features should be documented.

In most patients, a simple report of the absence of trauma is sufficient to eliminate the possibility of head injury. However, in any patient dependent on others, such as children, the elderly, and those requiring assistance in their activities of daily living, the absence of suspicious clues of occult trauma, such as abnormal behavior of the caregivers, should be noted. If child abuse is suspected, computed tomography (CT) is superior to magnetic resonance (MR) imaging to detect acute injury. However, MR gives more definitive information about the nature and extent of subacute and chronic injuries, without the risks of radiation.<sup>30</sup>

Bacterial meningitis can present subtly, and may initially resemble a viral upper respiratory tract infection. At a minimum, patients with fever and headache should

be thoroughly examined for the presence of a petechial rash and signs of meningeal irritation. Although the absence of Kernig and Brudzinski signs are often documented in patients with headache, both are rare and insensitive in meningitis.<sup>31,32</sup> In contrast, the jolt accentuation test, which is considered positive when headache pain is exacerbated by patients rotating their heads from side to side, has been found to be sensitive, and may be more helpful in identifying patients for further evaluation.<sup>33</sup> It is easy to overlook the importance of contiguous spread from surrounding head and neck structures; the absence of recent head and neck instrumentation and a full examination of the head and neck should be documented. The absence of severely ill contacts should also be noted, as should risk factors for immune compromise, both of which will lower the threshold for imaging and CSF examination.

CO poisoning is the most common poisoning in the United States and worldwide. It is life threatening and disabling, and remains commonly unrecognized and misdiagnosed. Headache that is associated with a flulike illness in the winter months when home furnaces are in use, similar symptoms in others within same residence, and a pattern of daily improvement after leaving the area of exposure are all clues that should heighten suspicion for CO poisoning.<sup>34–37</sup>

Temporal arteritis (TA) is a panarteritis that may be associated with polymyalgia rheumatica, a disease that results in chronic proximal muscle weakness in a predominantly older white female population. Prototypical symptoms of TA include bitemporal pain and jaw claudication, and ischemic pain with mastication that is relieved by rest. Classic physical findings include visual field deficits, temporal tenderness, and nodularity of the superficial temporal arteries on palpation. Although most patients do not present with these classic symptoms and signs, the majority do present with a new-onset headache, and almost all patients are more than 50 years of age.<sup>38,39</sup> Because of its natural progression to blindness that is preventable with treatment, TA should be considered in older patients with new-onset headaches.

Cervical artery dissection is a rare but potentially life-threatening cause of sudden-onset headache that may mimic SAH in its presentation. Carotid and vertebral artery dissections may occur spontaneously or may be precipitated by seemingly minor trauma, such as vigorous coughing or chiropractic manipulation. In carotid dissection, the pain may be unilateral, involving the face, and may be associated with pulsatile tinnitus or oculosympathetic palsy (miosis and ptosis).<sup>40</sup> In vertebral dissection, the pain is most commonly occipital or nuchal.<sup>41</sup> Although, in some cases, neurologic signs related to embolic events in the respective vascular territories may be present on the initial presentation, there is most commonly an interval of several days between the onset of headache and such events. Nonetheless, cervical artery dissection may be suspected clinically in a patient with new, sudden-onset headache if there is a history of a precipitating event, connective tissue disease, or a family history of unexplained ischemic stroke in younger or middle-aged relatives.<sup>40</sup>

Although most EPs would consider the diagnosis of preeclampsia in a pregnant woman who presents with a headache, many fail to do so in patients in the postpartum period. A large proportion of eclampsia and preeclampsia cases occur after delivery, and may result in permanent disability from cerebral infarction or death. Because headache is the most common presenting complaint in patients with postpartum preeclampsia, the onset of headache with new features at any time up to 4 weeks following delivery should prompt consideration of this diagnosis.<sup>42</sup>

Because it may present dramatically with severe headache, vomiting, and photophobia, acute angle-closure glaucoma is sometimes overlooked initially in the ED while time-consuming diagnostic investigations are performed to rule out SAH or meningitis. This time could be spent obtaining emergent ophthalmologic consultation

**Table 1****Critical headache diagnoses for the EP**

<b>Diagnosis</b>	<b>Critical Clinical Features</b>	<b>Critical Diagnostic Tests</b>	<b>Critical Interventions</b>	<b>Comments</b>
SAH	Sudden onset Maximal at onset Different than previous headaches	CT head LP	Neurosurgical consultation Blood pressure control Nimodipine Ventriculostomy	CT head and other neuroimaging modalities are insufficient to rule out the diagnosis
Occult trauma	Signs of abuse or neglect Anticoagulation or coagulopathy	CT head	Neurosurgical consultation Admission	Patients in at-risk populations may not volunteer a history of trauma
Bacterial meningitis	Fever Meningeal irritation Immune compromise Head and neck infection or instrumentation	CT head LP	Antibiotics Corticosteroids Isolation	Treatment should be initiated before diagnostic confirmation by CSF analysis if clinical suspicion is high. Corticosteroids should be initiated before or with the first dose of antibiotics in clinically apparent cases
TA	Jaw claudication Superficial temporal artery tenderness or nodularity Visual symptoms	Temporal artery biopsy	Systemic corticosteroids	ESR is an adequately sensitive screening test in patients without these high-risk features. Empirical corticosteroids are indicated in patients with high-risk features and findings or a markedly increased ESR
CO toxicity	Symptomatic cohabitants Flulike illness that is worse each morning Potentially toxic environment (eg, home furnace in winter)	Arterial cooximetry	HBOT	HBOT is indicated for patients with neurologic and cardiovascular signs and above certain cutoff levels
Acute glaucoma	Red eye Midrange fixed pupil Cloudy cornea	Intraocular pressure	Topical ocular therapy Systemic osmotic agents Ophthalmologic consultation	A cursory examination before neuroimaging should prevent costly delays in consultation and therapy

Cervical artery dissection	SAH-like onset Facial (carotid), neck (vertebral) pain Cranial nerve abnormalities	Angiography	Neurologic/ neurosurgical consultation Anticoagulation	In the absence of brain hemorrhage, anticoagulation is initiated to reduce the risk of thrombus formation and embolization
Cerebral/dural VST	Hypercoagulable state (pregnancy and puerperum, oral contraceptives, malignancy) Head and neck infection Proptosis (cavernous sinus thrombosis)	MR head Venography	Neurosurgical consultation Systemic anticoagulation	A D-dimer may be falsely negative
Space-occupying lesion	Progressively worse over time New onset in patient >50 years old History of malignancy Worse in morning Worse in head-down position	CT head	Neurosurgical consultation ICP-lowering therapies Lesion-specific therapies	Emergent ICP-lowering therapies may include elevating the head of the bed, restriction of intravenous fluids, mannitol, and hyperventilation Lesion-specific therapies may include emergent surgery/neuroradiological procedures, corticosteroids, and antimicrobial agents
Cerebellar infarction	Headache with dizziness Cerebellar signs Cranial nerve abnormalities	CT head	Neurologic/ neurosurgical consultation	Although CT head is insensitive for infarction, it is helpful initially to rule out hemorrhage and identify life-threatening edema and mass effect
Idiopathic intracranial hypertension	Obese, young female patient Cranial nerve 6 palsy (false localizing sign)	LP	CSF drainage Neurologic referral	After negative neuroimaging, an LP will reveal a markedly increased opening pressure and provide temporary headache relief
Pituitary apoplexy	Thunderclap headache Vomiting Visual acuity, field deficits Ocular palsies	CT head MR head	Neurosurgical consultation	Many pituitary infarctions and hemorrhages will not be easily visible on CT. MR is considered the diagnostic modality of choice
Preeclampsia	Postpartum (up to 4 weeks)	Complete blood count Chemistry panel with Liver function tests Coagulation studies	Intravenous magnesium Obstetric consultation	Up to half of all patients present in the postpartum period, the majority with a chief complaint of headache

*Abbreviations:* CSF, cerebrospinal fluid; CT, computed tomography; ESR, erythrocyte sedimentation rate; HBOT, hyperbaric oxygen therapy; ICP, intracranial pressure; LP, lumbar puncture; MR, magnetic resonance; TA, temporal arteritis; VST, venous sinus thrombosis.

and lowering intraocular pressure with topical and systemic therapy. Patients with acute angle-closure glaucoma will have ocular findings such as a unilateral red eye with decreased visual acuity, a fixed, midrange pupil, and corneal edema. A cursory examination before diagnostic studies that take the patient out of the ED are performed will prevent delays to critical interventions.

Space-occupying lesions include primary and secondary neoplasms, infectious processes such as brain abscesses and cysts, and vascular lesions such as unruptured giant cerebral aneurysms and arteriovenous malformations. Although this is a heterogeneous group of pathologies, headaches caused by space-occupying lesions share common features in their presentation; the sine qua non being a progressive and unremitting course as the lesion expands in volume and increases intracranial pressure (ICP). Headaches also tend to be worse with the head-down position, and in the morning after waking, when ICP is higher. The specific location of the lesion and its adjacent structures within the calvarium will determine other features of the presentation. Whether or not it is critical for the EP to uncover the presence of a space-occupying lesion differs from case to case. In the absence of neurologic findings on examination, a patient with a slowly progressive headache of several weeks' or months' duration may be appropriately discharged from the ED for urgent neuroimaging and follow-up in a primary care setting. On the other hand, patients at high risk for pathology, such as those with a history of malignancy, recent head and neck infection or surgery, immune compromise, or those more than 50 years of age with a new onset of headache, often receive neuroimaging in the ED. The discovery of a large lesion, or a lesion in a critical location, will sometimes lead to the initiation of emergency therapies to prevent further expansion, brain injury, and herniation. If neuroimaging is performed in the ED, CT is usually sufficient; space-occupying lesions that are only detectable on MR are unlikely to alter ED management.

Cerebral and dural VST is another rare, but life-threatening and treatable, cause of headache. The characteristics of the headache are variable, but some patients present with a thunderclap. Patients at risk for VST include those with hypercoagulable states, including pregnancy and the postpartum period, oral contraceptive use, and the nephrotic syndrome, head and neck infections, malignancies, and vasculitides.<sup>43-45</sup> Patients may present with signs of increased ICP, such as papilledema, and may continue to be symptomatic despite attempts at analgesia. If untreated, the thrombosis may progress to venous infarction and hemorrhage, which results in neurologic deficits that do not conform to an arterial territorial distribution. In some cases, VST eventually leads to brain herniation and death. Unless there are positive findings on the neurologic examination, there may be few other clues to compel the EP to pursue this diagnosis, and many cases go undiagnosed on the initial presentation.<sup>46,47</sup>

Idiopathic intracranial hypertension (IIH), previously known as pseudotumor cerebri, is a poorly understood disease with a predilection for obese middle-aged women. In these patients, a sustained increase in ICP seems to be related to an obstruction of CSF drainage at the level of the arachnoid granulations. However, in at least some cases coexistent VST is visible on contrast imaging studies, and, in this subgroup, more emergent therapy is necessary to prevent rapid deterioration.<sup>48,49</sup> In the absence of macroscopic thrombosis, deterioration is more gradual, with progressive visual-field deterioration occurring if ICP is not reduced. The physical examination most often reveals papilledema, and may reveal loss of peripheral visual fields. In some cases, a unilateral or bilateral sixth cranial nerve palsy is present. This palsy is a result of increased ICP, not a localized process, and thus is considered a false localizing sign. The diagnosis of IIH should be suspected in



patients with a headache pattern consistent with a space-occupying lesion who have negative neuroimaging studies. Although the diagnosis is not as time critical as with VST, it is strongly suggested by the finding of a grossly increased opening pressure during lumbar puncture (LP) that is accompanied by an immediate improvement in the patient's symptoms.

Pituitary apoplexy is an extremely rare cause of thunderclap headache. It is defined as hemorrhage or infarction of the pituitary gland, typically into a preexisting adenoma. Although headache may be the most prominent presenting complaint, pituitary apoplexy is most often accompanied by visual symptoms and signs, such as decreased acuity, reduction in visual fields, and ocular palsies.<sup>50</sup>

## PITFALLS OF DIAGNOSTIC TESTING

### *Relying on Neuroimaging to Rule out SAH*

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Despite advances in CT technology, noncontrast CT imaging alone remains inadequate to rule out nontraumatic SAH. In all but a single published case series,<sup>51</sup> an LP was required after a negative CT scan to make the diagnosis of SAH in a substantial minority of cases.<sup>52-58</sup> Although reported sensitivities in these case series typically exceed 90%, in practice, the sensitivity of CT for SAH is likely significantly lower, for several reasons. First and foremost is the critical issue of spectrum bias. Most studies begin their analysis with a group of patients ultimately diagnosed with SAH in hospital, potentially missing patients who are discharged from the ED and other outpatient settings with less severe presentations. These are precisely the patients in whom a timely diagnosis of SAH is so important to prevent a second, more severe bleed. In addition, most studies are conducted at referral centers, at which the equipment and the expertise of the radiologists are optimal. The ability of a general radiologist to detect small amounts of hemorrhage on CT is known to be inferior to that of a subspecialist neuroradiologist.<sup>59</sup> Lastly, small amounts of subarachnoid blood, after an initial leak, are rapidly absorbed; following the initial 12-hour interval after symptom onset, the sensitivity of CT decreases over time.<sup>60</sup>

Other imaging modalities, including MR, MR angiography, CT angiography, and conventional angiography, have not eliminated the need for LP with CSF analysis in cases of suspected SAH. MR is less sensitive than CT for the presence of blood in the first several hours after the onset of bleeding.<sup>30</sup> Even the addition of the fluid-attenuated inversion-recovery (FLAIR) technique, with its enhanced ability to detect blood, is insufficient. In a recent study of 12 patients with a negative CT scan who subsequently had SAH confirmed by CSF analysis, MR was only able to detect bleeding in 2.<sup>61</sup>

Although these technologies are continuing to evolve and improve, conventional angiography, CT angiography, and MR angiography are not 100% sensitive for the detection of cerebral aneurysms.<sup>62-65</sup> More importantly, angiography by any method is unable to distinguish between unruptured, asymptomatic aneurysms, which have an exceedingly low likelihood of rupture throughout a patient's lifetime, and symptomatic aneurysms that have already bled, and are likely to rebleed with serious consequences.<sup>66,67</sup> Thus, an LP with CSF analysis to confirm SAH can be critical to determine the need for surgical intervention when aneurysms are detected on angiography. Because the overall prevalence of cerebral aneurysms in the general population ranges from 2% to 6%,<sup>67</sup> the indiscriminate application of angiography to an unselected population of patients with headaches could result in unnecessary and harmful invasive procedures.

### ***Other Limitations of CT***

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CT is insensitive to detect VST. Although data are lacking to precisely estimate its sensitivity, in one consecutive series of 127 patients with VST, 17 patients who presented with isolated headache had normal brain CT scan and CSF examination.<sup>46</sup> The addition of contrast to CT will help identify some cases, but the diagnosis can only be ruled out using MR venography.<sup>68</sup> However, because of the rarity of this diagnosis, it is an unreasonable expectation for MR venography to be performed emergently in patients without neurologic findings unless risk factors and a strong clinical suspicion exist for VST.

Cerebellar infarction, like cerebral infarction, may not become apparent on CT scan for several hours. However, cerebellar infarction deserves special consideration by the EP because it is more likely to present as a headache without weakness or other localizing signs on neurologic examination.<sup>69</sup> Moreover, because of its location in the posterior fossa, there is a greater risk for brain herniation as the lesion evolves and edema ensues. Although CT is less sensitive than MR to visualize the contents of the posterior fossa, edema from cerebellar infarction is often visible. Distortion or obliteration of the fourth ventricle from the resultant mass effect should prompt neurosurgical consultation for possible decompression. Pituitary apoplexy, by contrast, is frequently not visualized on CT, and MR is advised if clinical suspicion for this entity exists.<sup>50</sup>

### ***Misinterpreting CSF Results***

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LP with CSF examination is critical in the evaluation of headaches suspicious for SAH or meningitis. In both instances, there are several common pitfalls that may interfere with a correct diagnosis. Within hours of the onset of subarachnoid bleeding, red blood cells (RBCs) are detectable in large numbers throughout the circulating CSF. In up to 15% of cases, LPs are traumatic, and RBCs from epidural vessels contaminate the specimen, making it difficult to identify a true SAH.<sup>70</sup> A common misunderstanding is that a progressive decrease in RBCs across serial collection tubes eliminates the possibility of SAH. Because SAH may coexist with RBCs that arise from a traumatic LP, the possibility of SAH can only safely be eliminated if the CSF count in one of the tubes approaches zero. If blood is encountered at the beginning of the LP, wasting the first 2 or 3 mL of fluid as the CSF clears will increase the likelihood that the RBC count will approach zero. If it does not, it may be necessary to repeat the procedure at a different interspace.

In cases in which traumatic LP makes the interpretation of RBC counts difficult, the presence of xanthochromia has been used to confirm the presence of true SAH. Xanthochromia is the yellowish discoloration of CSF that occurs in the hours following SAH as RBCs break down *in vivo* into bilirubin and oxyhemoglobin. However, xanthochromia has also been demonstrated to occur *in vitro* in collected specimens, resulting in falsely positive results.<sup>71</sup> Moreover, the practice of waiting until 12 hours have elapsed following the onset of headache, until the xanthochromia that develops *in vivo* is more reliably present, is not advised. Any advantage of this technique regarding the interpretation of CSF specimens is outweighed by the risk of a second aneurysmal bleed, which occurs more frequently in the hours immediately following the initial bleed than in any time period thereafter.<sup>72</sup> Almost all laboratories in the United States measure xanthochromia by visual inspection after centrifugation of the CSF specimen. Using this technique, falsely negative results are also possible.<sup>73</sup> Nonetheless, in patients who present several days after the onset of headache pain, xanthochromia

may be the only remaining sign of SAH on CSF analysis; it typically persists for 2 weeks.<sup>74</sup>

Although a negative LP effectively rules out the diagnosis of SAH,<sup>75</sup> it does not rule out other vascular emergencies that may result in a thunderclap headache, such as cervical artery dissection, cerebral and dural VST, cerebellar infarction, and pituitary apoplexy.

There are other important pitfalls of CSF interpretation in patients with a suspected central nervous system infection. It may be difficult to distinguish between bacterial and viral meningitis using the initial results of CSF analysis available in the ED. Although bacterial meningitis is more likely to result in high cell counts with a preponderance of polymorphonuclear leukocytes, a low glucose, and a positive Gram stain, none of these features is reliably present, and there is a significant overlap in CSF findings with viral meningitis. If sufficient clinical suspicion exists for bacterial meningitis, the most prudent course is to proceed with broad-spectrum antibiotic coverage until the results of bacterial cultures are available.

Certain populations, such as infants, the elderly, and those with immune compromise, may have a limited cellular response on initial CSF analysis. Moreover, in patients with suspected immune compromise, atypical pathogens, such as *Cryptococcus neoformans* and mycobacteria should be considered. Specific tests for these pathogens are necessary, and the collection of an additional tube of CSF for later use by the inpatient physician may be helpful.

In a traumatic LP, leukocytes should be present in small numbers in a fixed ratio with RBCs, typically in the range of 1 leukocyte for every 500 RBCs. This ratio may vary depending on the relative proportions of these cells in the peripheral blood. Although there is some evidence to support using such ratios to rule out meningitis in a traumatic tap, in the presence of large numbers of leukocytes and a high clinical suspicion for meningitis, it is advisable to repeat the LP at a different interspace.<sup>76</sup> It should also be noted that the most important treatable cause of viral encephalitis, herpes simplex encephalitis (HSE), may present with red cells and leukocytes in the CSF.<sup>77,78</sup>

### **Complications of LP**

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The most common complication of LP is a postural headache that can be persistent and debilitating, often resulting in repeat visits to the ED. These headaches occur in up to one-third of patients in some series, and usually occur within 3 days of the procedure. The headache is typically described as worse in the upright position, forcing patients to lie down; this is consistent with the theory that it is due to ongoing CSF leakage at the site of puncture and the resultant intracranial hypotension. Many of the traditional instructions given to patients to prevent post-LP headaches, including postprocedural bed rest, increased fluid intake, and caffeine administration, have little or no basis in evidence.<sup>79,80</sup> There is, however, sufficient evidence to support the practice of using a small (22 gauge), atraumatic (noncutting tip) needle to prevent post-LP headache.<sup>81,82</sup> Epidural blood patch, the injection of 5 to 30 mL of the patient's own blood into the epidural space at the site of the prior procedure, has been found to be an effective treatment of post-LP headache refractory to other therapies.<sup>83</sup>

The most feared complication of LP is brain herniation. Although it is rare, a strong temporal correlation between the procedure and subsequent herniation lends strength to a causal relationship.<sup>84</sup> Most investigators recommend performing a CT scan before LP to minimize this risk. Although a normal CT scan does not completely eliminate the risk of brain herniation with LP, in patients with mass lesions or other structural changes, an LP is not advised. Although there may be a small increase in the risk of deterioration or herniation from an unsuspected lesion, it may be acceptable to omit

the CT scan in selected patients with headache, such as those less than 60 years of age with no significant neurologic history and a normal neurologic examination.<sup>85,86</sup>

### ***Other Laboratory Pitfalls***

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CO cooximetry values may be misleading. Low or undetectable levels may not rule out CO poisoning in the patient who presents many hours after exposure, as CO clears from the blood over time. Even in toxic patients with high tissue levels that have accumulated over a long period of exposure, the administration of high-flow supplemental oxygen will accelerate clearance from the blood and may lead to levels in the normal or near-normal range.<sup>34,37</sup> If the diagnosis is strongly suspected, removal of the patient from the suspected toxic environment, and repeat testing with any recurrent symptoms, is advised.

Although erythrocyte sedimentation rate (ESR) is an invaluable screening test for TA in older adult patients with headache, in the presence of an extremely high pretest probability it is inadequately sensitive to rule out the diagnosis. Thus, in patients with jaw claudication, nodularity or tenderness over the superficial temporal artery, or diplopia, the diagnostic evaluation should not end with a normal, or only mildly increased, ESR. In patients with such suggestive clinical features, or those with less specific features but a highly increased ESR, empirical corticosteroids should be administered in the interval before a definite diagnostic determination is made with temporal artery biopsy.<sup>39</sup>

The dimerized plasmin fragment D (D-dimer) test may help to identify some patients with VST. However, its lack of specificity has been well documented, most notably in patients with identified risk factors for VST, such as women in the peripartum period, and patients with malignancy, vasculitis, and other chronic inflammatory conditions.<sup>87</sup> D-dimer is also falsely negative in a significant number of cases of VST diagnosed definitely with contrast neuroimaging studies, especially in patients who present with isolated headache.<sup>88-90</sup>

## **PITFALLS OF TREATMENT**

### ***Poor Analgesic Agent Choices***

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Several investigators have been critical of the patterns of analgesic use for headache in the ED setting. One criticism is directed at the lack of specificity of the agents used with respect to the underlying diagnoses, especially for migraine. Another is in regard to the frequency of opioid use, which is said to be too high and inconsistent with published consensus guidelines.<sup>3,91,92</sup> Many agents have been proven to be highly effective for acute headache in the ED, including migraine, and, in any given patient, there may be several acceptable choices. One of the key factors for the EP is the patient's previous response to the various agents available.

The dopamine antagonists, including droperidol, prochlorperazine, metochlopramide, and chlorpromazine, have a less well-delineated mechanism of action than the more migraine-specific DHE and triptans, which activate serotonin 1B/1D receptors. Nonetheless, these agents, when used alone<sup>93-99</sup> or in combination with other drugs,<sup>100</sup> have been shown to be equivalent or superior to drugs from all other classes in multiple controlled trials. Droperidol seems to be more efficacious than prochlorperazine,<sup>101,102</sup> which in turn seems to be more efficacious as a single agent than metochlopramide.<sup>103,104</sup> All agents are more effective when they reach the central nervous system quickly, with intravenous administration superior to the intramuscular and oral routes.<sup>104,105</sup>

Although not as effective overall as the dopamine antagonists, opioids are also successful at abating headache. Although they may be used in some cases for which other options are available, the treatment guidelines set forth by nonemergency medicine societies may not be an appropriate standard against which to evaluate ED practices. The patient population in the ED is unique. The more severe spectrum of acuity in the ED, the lower likelihood of diagnostic precision, and the fact that many patients have already tried 1 or more medications before being evaluated, all suggest that different practice patterns are to be expected. Nonetheless, wide regional differences among EPs, and the discrepancy between their responses to hypothetical scenarios and actual practices observed, indicate that other factors also play a role.<sup>106,107</sup>

Patients who visit the ED frequently with a chief complaint of headache are often stigmatized by EPs and ED staff. These patients, who make up a larger proportion of patients in the ED than in office-based and specialty clinic settings are often labeled as drug-seekers.<sup>18</sup> They often request specific medications and are more frequently prescribed opioids. They also have a higher frequency of chronic headaches, and a large proportion use symptomatic headache therapies on a daily or almost daily basis, especially combination preparations containing opioids and caffeine, a syndrome known as medication overuse headache. Higher rates of opioid use in the ED may reflect, in part, the refractoriness of such patients to other therapies.<sup>18</sup>

With so many efficacious therapies available, pitfalls are more commonly related to medication side effects. The EP must therefore be mindful of a few key contraindications and complications of the commonly used agents. The dopamine antagonists are notable for prolonging the QT interval on the electrocardiogram (ECG). Moreover, it is not uncommon for 2 agents to be used that each cause some degree of QT prolongation, such as ondansetron for nausea, combined with a dopamine antagonist. Although this is rarely of clinical consequence, in patients with preexisting conduction or electrolyte abnormalities, or those who are already receiving therapy with other agents that prolong the QT interval, it can sometimes lead to torsades de pointes (TdP), a potentially fatal dysrhythmia. Women, who are disproportionately represented among patients with migraine headache, are at higher risk than men.<sup>108</sup> The relationship between QT-prolonging agents and TdP is unclear, and seems to be nonlinear. Agents that cause only minimal prolongation of the QT interval may cause TdP at higher rates than those that cause more marked prolongation.<sup>108</sup> Because patients with cardiac or electrolyte abnormalities are known to be at higher risk, it may be prudent to avoid dopamine antagonists in these patients, or to monitor them with telemetry or serial ECGs during therapy.

The other, more common but less life-threatening, concern with the dopamine antagonists is akathisia, an uncomfortable sensation of not being able to sit still. It occurs with varying severity in a substantial minority of patients.<sup>109</sup> In general, it has not limited the ability of this class of agents to be effective, and when severe, it is reliably abated by the use of anticholinergic agents such as diphenhydramine.<sup>109</sup> The incidence of akathisia may be decreased by the use of slower infusion rates,<sup>110</sup> or by using an anticholinergic premedication.<sup>111</sup>

The triptans offer greater selectivity for serotonin receptors, and are available for administration by oral and subcutaneous routes. They have largely replaced DHE in the primary care and neurology specialty clinic settings. However, DHE is still in use in many EDs, possibly because of its low cost and availability as an intravenous preparation. Most investigators recommend avoiding DHE in patients with cardiovascular disease, uncontrolled hypertension, and in pregnancy.<sup>112</sup> Although triptans have been shown to be more efficacious than DHE,<sup>113</sup> many EPs have lingering concerns about their cardiovascular risk, and are concerned about the frequent occurrence of chest

pain and pressure that occurs after their administration. Although there is evidence that these symptoms are not cardiac related,<sup>114</sup> coronary vasospasm has been documented in the catheterization laboratory with the administration of triptans in patients with diseased coronary arteries.<sup>115</sup> Moreover, most subjects studied to establish the safety of triptans have been those without evidence of cardiac disease. It is thus recommended that these agents be avoided in patients with a history of coronary artery disease.

### ***Withholding Empirical Antibiotics and Steroids in Suspected Meningitis***

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In patients clinically suspected of having bacterial meningitis, such as those who appear ill and are febrile with signs of meningeal irritation, broad-spectrum antibiotics should not be withheld pending the results of diagnostic studies. Bacterial meningitis progresses rapidly, and outcomes are most likely related to the time to antibiotic administration in patients with overt presentations.<sup>116–118</sup> Moreover, a short interval of antibiotics before LP is unlikely to obscure the diagnosis on CSF analysis.<sup>119</sup>

Corticosteroids have also been shown to reduce mortality and improve outcomes in patients with bacterial meningitis when they are administered before, or concurrently, with antibiotics. Their empirical administration should similarly be considered in patients in whom bacterial meningitis is strongly suspected.<sup>120,121</sup> Because many patients in the United States receive empirical antibiotics before CSF examination based on a low or moderate clinical suspicion, coadministering a large dose of corticosteroids in all of these patients may expose the majority, who do not have meningitis, to unnecessary risks. There are limited data to address this question; the best approach may be to limit empirical steroid administration to those patients in whom meningitis is most strongly suspected.

After CSF results become available, additional antimicrobial therapy may be indicated to cover specific organisms and possible drug-resistant strains, especially in special at-risk populations.<sup>122,123</sup> Acyclovir should be added to the empirical treatment regimen for patients with CSF pleocytosis and a negative Gram stain until the results of more definitive tests are available, such as the polymerase chain reaction test for the herpes simplex virus.<sup>77</sup>

## **PITFALLS OF DISCHARGE AND FOLLOW-UP MANAGEMENT**

### ***Poor Discharge Planning***

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Although many patients leave the ED pain free, recurrence of headache in the day following the ED visit is a common problem occurring in most discharged patients with a diagnosis of migraine in one study,<sup>124</sup> and in almost one-third of patients with primary headaches in another.<sup>125</sup> It is important to consider the patient's previous history of headache recurrence during discharge, as repeat ED visits can be avoided in many cases. Risk factors associated with recurrence of moderate to severe pain and functional impairment within 24 hours of discharge include incomplete resolution at discharge,<sup>124,126</sup> severe baseline pain, a longer duration of pain, baseline nausea, and a positive screen for depression.<sup>125</sup> In patients who obtain headache relief with intramuscular sumatriptan, discharge with an oral dose, to be used in the event of recurrence, is appropriate.<sup>127</sup> In other patients, the use of nonsteroidal antiinflammatory agents, acetaminophen, aspirin, or oral antiemetics at the first sign of recurrence may be helpful. Several randomized, controlled studies have looked at the role of oral or intravenous dexamethasone to reduce the rate of headache recurrence. Although several of these studies were negative,<sup>126,128–130</sup> a recent meta-analysis<sup>131</sup> found an overall benefit of parenteral dexamethasone at 72 hours posttreatment. Although it

is difficult to recommend the routine use of corticosteroids, they seem to have a role, and may be especially useful in those patients with a headache of greater than 72 hours duration before presentation.<sup>130</sup>

Patients should be given follow-up care with a primary care provider. In certain cases that present a diagnostic or therapeutic challenge, neurologist or headache specialist follow-up may also be warranted. It is important for patients to be instructed to return to the ED if their symptoms worsen or if new symptoms evolve; many of the dangerous diagnoses discussed earlier may initially present as an isolated headache but go on to develop additional symptoms and signs as they progress.

Patients who visit the ED frequently with exacerbations of primary headache present a special challenge. Although there are few data to describe successful strategies for their ED management, consistency in their care among EPs and other ED staff, and regular communication among EPs, primary care providers, and specialists, may improve their outcomes.

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