

*Clinical Policy:  
Critical Issues in the Evaluation  
and Management of Patients  
Presenting to the Emergency Department  
with Acute Headache*

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# Clinical Policy: Critical Issues in the Evaluation and Management of Patients Presenting to the Emergency Department With Acute Headache

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This clinical policy focuses on critical issues in the evaluation and management of patients with acute headache. A MEDLINE search was performed, abstracts were reviewed, and appropriate full-text articles were read; references from reviewed articles were searched for additional material. This policy focuses on 4 areas of current interest and/or controversy in acute headache management: (1) response to headache therapy as an indicator of underlying pathology, (2) clinical findings predictive of increased intracranial pressure, (3) indications for emergent neuroimaging in patients with a complaint of headache, and (4) indications to pursue emergent diagnostic studies in patients with thunderclap headache but with normal findings on a head computed tomography (CT) scan and negative findings on a lumbar puncture. Recommendations for patient management are provided for each of these 4 topics based on strength of evidence. Level A recommendations represent patient management principles that reflect a high degree of clinical certainty, Level B recommendations represent patient management principles that reflect moderate clinical certainty, and Level C recommendations represent other patient management strategies based on preliminary, inconclusive, or conflicting evidence, or based on panel consensus. This guideline is intended for physicians working in hospital-based emergency departments.

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## INTRODUCTION

Headache is a common complaint for which patients seek emergency department care. The diagnoses for patients with headache range from non-life-threatening proc-

esses such as migraine to life-threatening conditions such as subarachnoid hemorrhage (SAH). Missing a life-threatening condition may result in adverse patient outcomes and may also pose the potential for medicolegal liability. For these reasons, the American College of Emergency Physicians (ACEP) chose headache as a clinical policy topic. The original headache clinical policy was published in June 1996.<sup>1</sup> The format of the initial headache clinical policy focused on the evaluation of a patient presenting with a chief complaint of headache as opposed to specific disease processes. It was a broad-based attempt to focus on key history, physical, and diagnostic findings to drive the diagnosis of potentially serious medical conditions with emphasis on SAH, meningitis, and carbon monoxide poisoning. Because of the all-inclusive nature of the previous policy, the format did not allow specific emphasis on critical issues in the evaluation of selected subsets of headache patients.

The Clinical Policies Committee believes that the format of the previous complaint-based clinical policy has gone as far as possible in directing the appropriate evaluation and treatment of patients presenting with headache. The committee is satisfied that the previous policy met the original goals of ACEP. This has been exemplified by the use of clinical policies to direct physician education and research, its use by quality improvement personnel in individual hospitals, its use in medical malpractice cases for establishing a reasonable standard of care, and its use by private companies in creating templates for physician history and physicals. A decision was made to develop a revised policy that focuses on critical issues in the evaluation and management of patients with a chief complaint of acute headache. It is hoped that departure from the previous format will improve patient care and direct critical areas of future research.

This policy is not intended to be a complete manual on the initial evaluation and management of patients with headache. Specifically, some areas of interest to the practicing emergency physician were not addressed because committee members believed either that there was not enough evidence to pursue an analysis of the topic or that the topic had been extensively discussed in recent literature and did not warrant additional discussion at this time. An example of this is the sensitivity of computed tomography (CT) in diagnosing SAH.<sup>2</sup>

The reasons for developing clinical policies in emergency medicine and the approaches used in their development have been enumerated.<sup>3</sup> This policy is a product of the ACEP clinical policy development process, includ-

ing expert review, and is based on the existing literature. Expert review comments were received from emergency physicians; physicians from other specialties, such as neurologists; and specialty societies, including members of the American Academy of Family Physicians, American Academy of Neurology (AAN), American Headache Society, American Society of Neuroimaging, and the National Headache Foundation. Their responses were used to further refine and enhance this policy. Clinical policies are scheduled for revision every 3 years; however, interim reviews are conducted when technology or the practice environment changes significantly.

### Methodology

This clinical policy was created after careful review and critical analysis of the peer-reviewed literature. A MEDLINE search for articles published between January 1966 and December 1999 was performed using combinations of the following key words: headache and pathophysiology, or mechanisms: lumbar puncture or spinal tap, or dural puncture and herniation, or complications, or headache, or subarachnoid hemorrhage: headache and computed tomography, magnetic resonance imaging, or diagnostic testing: thunderclap headache and diagnostic testing or subarachnoid hemorrhage. Searches were limited to English-language sources. Additional papers were reviewed from the bibliography of articles cited. Recent journals and standard texts were also examined for additional sources.

Pertinent articles were selected from the reviewed abstracts and from bibliographies of initially selected papers. Publications were stratified by at least 2 of the subcommittee members into 1 of 3 categories of strength of evidence according to the following criteria:

**Strength of evidence Class I**—Interventional studies including clinical trials, observational studies including prospective cohort studies, aggregate studies including meta-analyses of randomized clinical trials only.

**Strength of evidence Class II**—Observational studies including retrospective cohort studies, case-controlled studies, aggregate studies including other meta-analyses.

**Strength of evidence Class III**—Descriptive cross-sectional studies, observational reports including case series and case reports, consensus studies including published panel consensus by acknowledged groups of experts.

Strength of evidence Class I and II articles were then rated on elements the committee believed were most important in creating a quality work. Class I and II articles with significant flaws or design bias were downgraded

from 1 to 3 levels based on a set formula. Strength of evidence Class III articles were downgraded 1 level if they demonstrated significant flaws or bias. Articles downgraded below a Class III strength of evidence were given an “X” rating and were not used in formulating this policy.

Articles were assembled into evidentiary tables that were used to answer the 4 questions posed in this clinical policy, and recommendations regarding patient management were then made according to the following criteria:

**Level A recommendations.** Generally accepted principles for patient management that reflect a high degree of clinical certainty (ie, based on “strength of evidence Class I” or overwhelming evidence from “strength of evidence Class II” studies that directly address all the issues).

**Level B recommendations.** Recommendations for patient management that may identify a particular strategy or range of management strategies that reflect moderate clinical certainty (ie, based on “strength of evidence Class II” studies that directly address the issue, decision analysis that directly addresses the issue, or strong consensus of “strength of evidence Class III” studies).

**Level C recommendations.** Other strategies for patient management based on preliminary, inconclusive, or conflicting evidence, or, in the absence of any published literature, based on panel consensus.

There are certain circumstances in which the recommendations stemming from a body of evidence should not be rated as highly as the individual studies on which they are based. Factors such as heterogeneity of results, uncertainty about effect magnitude and consequences, strength of prior beliefs, and publication bias, among others, might lead to such a downgrading of recommendations.

### Scope of Application

This guideline is intended for physicians working in hospital-based EDs.

## CRITICAL QUESTIONS

### I. Does a response to therapy predict the etiology of an acute headache?

**Background.** Because headache is a common complaint, physicians have looked for ways to differentiate the life-threatening etiologies from the more benign ones. Defining who can be sent home safely without further work-up could improve patient care while decreasing patient cost. Review of the literature suggests that some clinicians have tried to use response to medications as an indicator of the seriousness of a patient’s headache. To fully address this question, it is important to understand the underlying

pathophysiologic characteristics of headache pain and the pharmacologic rationale behind the current concepts in therapy.

Current understanding of headache suggests that there is a common pathway for the pain regardless of the underlying etiology. Much of our understanding regarding the pathophysiologic characteristics comes from research on migraine headache. In essence, headache can be caused by (1) distention, traction, or dilation of intracranial or extracranial arteries, (2) traction or displacement of large intracranial veins or the dural envelope, (3) compression, traction, or inflammation of cranial and spinal nerves, (4) spasm, inflammation, and trauma to cranial and cervical muscles, (5) meningeal irritation and raised intracranial pressure, and (6) disturbance of intracerebral serotonergic projections.<sup>4</sup>

There is evidence to suggest that headache pain is transmitted via the trigeminal nerve from the blood vessels of the pia mater and dura mater.<sup>5</sup> The exact trigger of the pain may be multifactorial, but, once the trigger occurs, the trigeminovascular axons are stimulated, resulting in the onset of pain and release of neurogenic peptides stored in the afferent C fibers innervating cephalic blood vessels. These vasoactive neuropeptides then stimulate endothelial cells, mast cells, and platelets, creating an inflammatory cascade known as “neurogenic inflammation.” Vasodilatation with enhanced permeability of plasma proteins follows with a perivascular inflammatory reaction.<sup>6</sup> “Neurogenic inflammation” within the cephalic tissue is one model that has been proposed as the pathogenic mechanism of headache. However, selective and potent inhibitors of “neurogenic inflammation” have thus far proven ineffective in clinical trials.

Serotonin (5-HT) receptors are the main focus of pain management because they are known to modulate neurogenic peptide release and vasoconstrict dilated dural vessels.<sup>7</sup> The goal of therapy is to prevent or abort the neurogenic inflammation that occurs as a result of neuropeptide release. The 5-HT<sub>1</sub> receptor is believed to be the most important of the subtype receptors in the final common pathway of headache. 5-HT itself, despite many adverse effects, is a potent vasoconstrictor that makes it an effective treatment in migraines. Pharmacologic agents with an affinity for 5-HT receptors are currently the preferred therapy in acute headache management. Some agents, such as the triptans, are specific agonists at the 5-HT<sub>1</sub> receptor, whereas other medications, such as dihydroergotamine, prochlorperazine, and metoclopramide, act at a variety of serotonin and other aminergic receptors.<sup>4,8</sup>

**Findings.** There are no prospective randomized controlled trials, evidence from meta-analysis from random-

ized controlled trials, or well-designed cohort studies to support or refute the practice of using response to therapy in nontraumatic headaches as an indicator of potential underlying pathologic entities. The only published data regarding response to pain medications as an indicator of underlying headache etiology is in the form of case reports.

Seymour et al<sup>9</sup> described 3 headache patients who were eventually found to have significant intracranial pathologic hemorrhage after initial release from the ED after successful treatment with nonnarcotic analgesics. One woman was treated with ketorolac, improved, and was discharged with antibiotics and oral narcotics. The following day she was found unresponsive with a CT scan revealing a large intracerebral hemorrhage. Another woman presented with a pounding bitemporal headache and an elevated blood pressure; she was treated and discharged after initial improvement from prochlorperazine, lorazepam, nifedipine, and ibuprofen. She returned 3 days later with worsening headache and nuchal rigidity. An emergent CT scan revealed an SAH. The third patient was diagnosed with a muscle tension headache that was treated with ibuprofen, ketorolac, and prochlorperazine. The patient returned 24 hours later, at which time the evaluation revealed an intracerebral hemorrhage.

Gross et al<sup>10</sup> reported on 2 cases of viral meningitis and 1 case of meningeal carcinomatosis in which patients described complete pain relief with dihydroergotamine and metoclopramide. Lipton et al<sup>11</sup> described a case in which a carbon monoxide–induced headache was completely relieved with sumatriptan.

### Patient management recommendations.

**Level A recommendations.** None specified.

**Level B recommendations.** None specified.

**Level C recommendations.** Pain response to therapy should not be used as the sole diagnostic indicator of the underlying etiology of an acute headache.

### II. In which adult patients with a complaint of headache can a lumbar puncture be safely performed without a neuroimaging study?

**Background.** In the patient with an acute headache, head CT and cerebral spinal fluid (CSF) analysis are used alone and in combination to diagnose life-threatening entities including mass lesions, intracranial hemorrhage, and infections. There are times when CSF analysis alone would suffice, however, concern of causing herniation often prompts obtaining a head CT scan before a lumbar puncture (LP).

To choose the appropriate diagnostic study, it is important to know the indications and limitations of the study. If a CSF analysis is the only test needed, it is important to recognize which patients can have an LP safely performed without risk of herniation.

The limitations of CT include: (1) The technical inability of scanners to identify small hemorrhages in areas obscured by artifact or bone, (2) the inability to diagnose idiopathic intracranial hypertension, meningitis, or carotid or vertebral artery dissection, (3) the varied levels of expertise of the reader, and (4) the radiologic dilution that occurs as CSF flows through the subarachnoid space. Concentrations of hemoglobin less than 10 g/dL will appear isodense and are easily overlooked by the reviewer.<sup>12</sup> The LP also has well-defined limitations including significant intracranial pathologic entities, which can present in a manner similar to SAH, such as an unruptured aneurysm or sinus venous thrombosis, and may not be identified if only an LP is performed. The LP is time-consuming and can be technically difficult in uncooperative or obese patients. Contamination of the CSF with venous blood introduced during the technique may make interpretation of CSF difficult. Finally, there is morbidity including post–dural puncture headache.<sup>13</sup>

The risk of herniation has been the paramount concern of clinicians who perform LPs. The earliest description of this complication was reported 6 years after Heinrich Quincke performed the first LP in 1890.<sup>13</sup> Four deaths resulting from herniation were reported by Furbinger in 1896; the increased intracranial pressure was attributed to cerebellar neoplasms in 2 cases, to a cerebellar abscess in 1 case, and to a frontal tumor in 1 case.<sup>13</sup> Although herniation is a rare occurrence overall, other case reports have been published since these earliest observations describing cerebral herniation resulting from the performance of an LP.<sup>14</sup>

**Findings.** The safety of performing an LP before a neuroimaging study in patients with a chief complaint of headache has not been tested prospectively. For ethical reasons, it is unlikely that patients with focal neurologic findings, altered mental status, or other evidence of increased intracranial pressure are likely to ever be enrolled as subjects in a controlled trial in which an LP would be done before a neuroimaging study.

Two case series by Duffy<sup>15,16</sup> describe occurrences of herniation in patients with known or strongly suspected intracranial hematomas. In 1 report, 10 of 30 patients stopped breathing or developed unequal pupils while the needle was still in place or shortly after it was removed.<sup>15</sup> Fifteen of the 30 patients had marked deterioration within 24 hours of the procedure. The relative contributions

of the LP versus the natural disease course to the patient's clinical deterioration is not known. All 30 patients in this report had significant clinical findings such as a focal neurologic examination, progressive mental status changes, papilledema, "meningitic symptoms," or abnormal cranial radiographs. In another case series, 44 of 74 patients underwent LP before neuroimaging.<sup>16</sup> All of the patients were drowsy, confused, or had neurologic deficits. Seven had clinical deterioration at the time of LP, and all of these had an intracranial hematoma.

A case series reported from southern Australia in 1985 described LP in 70 patients who had either a "mild hemiparesis," drowsiness, or who were confused.<sup>17</sup> Only one of the 70 patients, a patient with an SAH, deteriorated after the LP and died 12 days later.

Whereas Duffy's case series suggests the high likelihood of an adverse outcome if a patient with a space-occupying lesion undergoes an LP, a 1988 report by Zisfein and Tuchman<sup>18</sup> had the opposite finding. Thirty-eight patients with head CT scans demonstrating an intracranial mass underwent LP "to rule out meningitis." All patients had an abnormal mental status or focal neurologic examination before undergoing the procedure. Thirty-four patients (89%) had evidence of a mass effect on head CT scanning. The central nervous system (CNS) pathologic characteristics included hematomas, abscesses, and dural collections. No significant neurologic deterioration was noted in 37 of 38 patients. One patient who had no brainstem function (absent caloric reflexes, dilated and fixed pupils) before the LP died after the procedure.

Patients with a headache, a normal neurologic examination, a normal mental status, a normal funduscopic examination, and no meningeal signs are theoretically the best candidates for the "LP without CT" paradigm. To characterize patients who could safely undergo an LP, researchers at Duke University Medical Center asked internal medicine residents, with ED attending supervision, to complete standard forms before CT scan of all patients who presented to the ED and needed an emergent LP.<sup>19</sup> The reasons for emergent LP were suspected meningitis (37%), suspected SAH (42%), and other (21%). The physicians were also asked to record their impression of the likelihood that a patient would have a CT finding that contraindicated dural puncture. Seventeen of 111 enrolled patients had a new CNS abnormality. Three of 17 had contraindications to spinal tap. Clinical findings that predicted abnormal CT results with statistical significance were altered mental status (positive likelihood ratio 2.2; 95% confidence interval [CI] 1.5 to 3.2), papilledema (positive likelihood ratio 11.1; 95% CI 1.1 to 115), and focal neurologic findings (positive likelihood ratio 4.3;

95% CI 1.9 to 10). The physicians' clinical impression had the highest predictive value in identifying patients with a contraindication to LP (positive likelihood ratio 18.8; 95% CI 4.8 to 43). Clinicians identified the 3 patients with contraindications to LP. Clinical attributes, including the diagnosis of HIV disease or having HIV risk factors, history of a CNS mass lesion, or a history of malignant neoplasm, were not statistically significant in predicting patients in whom an LP was contraindicated. This finding is likely a consequence of the study's small sample size. The study did not specifically address patients suspected of SAH nor did it provide outcome data using an "LP first" paradigm; therefore, a uniformly favorable result cannot be assumed without prospective validation studies.

### Patient management recommendations.

**Level A recommendations.** None specified.

**Level B recommendations.** None specified.

**Level C recommendations.** Adult patients with headache exhibiting signs of increased intracranial pressure including papilledema, absent venous pulsations on funduscopic examination, altered mental status, or focal neurologic deficits should undergo a neuroimaging study before having an LP.

In the absence of findings suggestive of increased intracranial pressure, an LP can be performed without obtaining a neuroimaging study. (Note: An LP does not assess for all causes of a sudden severe headache.)

### III. Which patients with headache require neuroimaging in the ED?

**Background.** It is estimated that only 1% of patients presenting to the ED with a complaint of headache have significant underlying pathologic characteristics that require emergent, or at least urgent, diagnosis.<sup>20</sup> The emergency physician is tasked with the responsibility of determining who needs neuroimaging in the ED versus who can be appropriately evaluated in the outpatient setting. Unfortunately, this task is made more difficult by societal factors that limit access to outpatient care for many of our patients. Further complicating the issue is the outcome measure one uses in determining the need for neuroimaging in the ED, that is, diagnosis for disposition versus identification of life-threatening etiologies. For example, diagnosing a brain tumor may not require immediate neurosurgery or even hospitalization yet may clearly direct the disposition and follow-up timing of the patient.

ACEP, the AAN, the American Association of Neurological Surgeons, and the American Society of Neuroradi-

ology have categorized neuroimaging into *emergent*, *urgent*, and *routine*.<sup>21</sup> *Emergent studies* are those essential for a timely decision regarding potentially life-threatening or severely disabling entities. *Urgent studies* are those that are arranged prior to discharge from the ED (scan appointment is included in the disposition) or performed prior to disposition when follow-up cannot be assured. *Routine studies* are indicated when the study is not considered necessary to make a disposition in the ED.

The primary focus in obtaining a neuroimaging study in the ED is to identify a treatable lesion. Treatable lesions include tumors, arterial venous malformations, aneurysms, SAH, cerebral sinus thrombosis, subdural and epidural hematomas, and hydrocephalus. These positive findings provide tangible outcomes that can be clearly assessed from a clinical and financial perspective. Less tangible is the impact of reassurance to the patient who has a normal study. In 1 study, 60% of patients presenting with headache had concerns of harboring significant pathologic findings and 40% of those reassured that they had no reason for concern left questioning their evaluation.<sup>22</sup>

The need for neuroimaging in headache patients has been addressed in at least 3 practice guidelines during the past decade. In 1994, the AAN published a “Practice Parameter: The Utility of Neuroimaging in the Evaluation of Headache in Patients With Normal Neurologic Examinations.”<sup>23</sup> This evidence-based document identified 17 pertinent studies, graded their methodology, and made 3 recommendations with “moderate clinical certainty.” (1) neuroimaging is not warranted in patients with a diagnosis of migraine who present with a typical event, (2) neuroimaging should be considered in patients with atypical headaches, history of seizures, or focal neurologic signs or symptoms, and (3) there is insufficient evidence to define the role of CT versus magnetic resonance imaging (MRI) in headache patients without a migraine headache.

In 1996, ACEP published the “Clinical Policy for the Initial Approach to Adolescents and Adults Presenting to the Emergency Department With a Chief Complaint of Headache.”<sup>1</sup> This was in essence a consensus document that did not take a strict evidence-based approach to decisionmaking. Regardless, the authors did grade the literature and recommended CT as a “rule” for patients with severe, sudden-onset headache, suspected intracranial infection, and neurologic deficits. CT was recommended as a “guideline” for a large number of historical or physical findings, thus recognizing the need to place the patient’s complaint in the general context of the presentation.

In 2000, the US Headache Consortium provided “Evidence-Based Guidelines in the Primary Care Setting: Neuroimaging in Patients with Nonacute Headache.”<sup>24</sup>

This document reached 5 main conclusions: (1) neuroimaging should be considered in patients with nonacute headache and an unexplained abnormality on neurologic examination, (2) there is insufficient evidence to make neuroimaging recommendations based on the presence or absence of neurologic symptoms (of note, this guideline addresses chronic headache rather than acute), (3) neuroimaging is usually not warranted in patients presenting with a typical migraine headache with no neurologic deficits, (4) there is insufficient data for an evidence-based recommendation on the use of neuroimaging for tension-type headaches, and (5) there is insufficient data for evidence-based recommendations regarding CT versus MRI in the evaluation of nonacute headache.

**Findings.** No well-designed, prospective studies were identified that definitively described the historical or clinical features of those patients with a life-threatening etiology of their headache. Consequently, no “Level A recommendations” can be generated regarding neuroimaging of the ED patient with a headache. Indeed, on initial assessment, there appeared to be considerable contradictions in the literature regarding the positive predictive value of some findings. For example, some studies identified “worst headache of one’s life” as predictive of an SAH,<sup>25,26</sup> whereas other studies did not find this complaint useful in differentiating those patients with SAH from those without SAH.<sup>27,28</sup>

The cornerstone to assessing the patient with a headache is the history and physical. Although this seems obvious, it is worth emphasizing because no decisionmaking can take place without appropriate data. The vast majority of articles reviewed failed to define how historical and physical information was collected. Because most of the studies were retrospective in design, it is fairly certain that there was no standardization in assessing the patients. The 1994 practice parameter by the AAN began by excluding those patients with abnormal findings in their neurologic examinations, thus implying that those patients with a headache and abnormal examination results require neuroimaging.<sup>23</sup> Indeed, entry criteria for many of the studies reviewed required the presence of normal findings in a neurologic examination.<sup>25,29,30</sup>

The US Headache Consortium, in their review of articles dealing with chronic headache, calculated likelihood ratios for patients presenting with headache and focal neurologic findings.<sup>24</sup> They reported that the presence of an abnormality on the neurologic examination increased the likelihood of positive results in a neuroimaging study threefold (95% CI 2.3 to 4.0). Normal findings in a neurologic examination reduced the odds of positive findings in a neuroimaging study by 30%. Ramirez-Lassepas et

al<sup>31</sup> retrospectively reviewed the records of 468 patients who presented to the ED with a chief complaint of headache. The authors reported that abnormal findings in a neurologic examination had a positive predictive value for intracranial pathology of 39%.

Historical findings that have prompted neuroimaging in headache patients include age older than 50 years,<sup>31-33</sup> occipital location,<sup>31</sup> worsening of headache with valsalva,<sup>33</sup> headache waking patient up,<sup>27,33</sup> and headache associated with syncope, nausea, or sensory distortion.<sup>27</sup> The US Headache Consortium calculated likelihood ratios for each of these symptoms and, based on the best available evidence in the literature, found that these symptoms may increase the probability of positive findings in a neuroimaging study but reported that the CIs are so wide that clear recommendations could not be made. There is not enough evidence regarding patients with acute onset headache and these symptoms to make any recommendation at this time.

Two subsets of headache patients deserve special mention: those presenting with acute sudden-onset headache, and HIV-positive patients presenting with a new or different headache. Acute sudden-onset headache prompts concerns for a cerebrovascular accident (eg, SAH). Mitchell et al<sup>27</sup> reported on 27 patients with the “worst headache of their life,” and only one had intracranial pathology. Ramirez-Lassepas et al<sup>31</sup> reviewed 468 headache patient records and found no association between the type of headache and the final diagnosis. Reinius et al<sup>34</sup> retrospectively studied 333 patients with an acute headache; 17 presented with the “worst headache of their life” complaint, yet only 1 had positive findings when a head CT scan was performed (LP results were not reported). Conversely, Harling et al<sup>26</sup> prospectively studied patients presenting with a thunderclap headache; of 49 patients, 35 had an SAH. Lledo et al<sup>25</sup> prospectively studied all patients presenting with acute sudden-onset headache with no past history over a 1-year period. Of 27 patients enrolled, 9 had SAH, 1 had intraventricular hemorrhage, and 2 had meningitis. Interestingly, only 4 of the 9 had positive CT results. In a prospective study, Mills et al<sup>28</sup> reported that 29% of patients complaining of the “worst headache of their life” had positive findings when a head CT was performed. All of these studies suffer to some degree from methodologic flaws. Although neither sensitive nor specific, there is sufficient evidence to support using acute sudden-onset headache as an important historical finding associated with an acute vascular event.

Patients with HIV disease frequently have CNS processes that include space-occupying lesions. Lipton et al<sup>35</sup>

reported on 49 HIV patients presenting with a chief complaint of headache, 35% of whom were found to have a mass lesion. Rothman et al<sup>36</sup> prospectively studied 110 HIV patients with neurologic complaints searching for predictors of new focal CNS lesions. Twenty-four percent of the patients were found to have a focal lesion. Using multivariate logistic regression analysis, new seizure, depressed or altered orientation, and headache that was different in character or lasted more than 3 days, all patients with a focal lesion were identified. As reported on other headache studies, focal motor deficit had a strong univariate association, with a positive predictive value of 41.7 and a *P* value of .02.

#### Patient management recommendations.

**Level A recommendations.** None specified.

**Level B recommendations.** Patients presenting to the ED with headache and abnormal findings in a neurologic examination (ie, focal deficit, altered mental status, altered cognitive function) should undergo emergent\* noncontrast head CT scan.

Patients presenting with acute sudden-onset headache should be considered for an emergent\* head CT scan.

HIV-positive patients with a new type of headache should be considered for an urgent\* neuroimaging study.

**Level C recommendations.** Patients who are older than 50 years presenting with new type of headache without abnormal findings in a neurologic examination should be considered for an urgent neuroimaging study.

#### IV. Is there a need for emergent angiography in the patient with a “thunderclap headache” who has negative findings in both CT and LP?

**Background.** The term thunderclap headache is used to describe a sudden-onset headache of excruciating pain that reaches its maximal intensity within seconds. These headaches suggest the presence of an SAH. The customary workup for SAH involves a noncontrast CT scan and an LP looking for blood or xanthochromia. The current teaching is that, if both tests yield negative results, SAH is ruled out.<sup>37</sup> The timing of the LP may be critical in this decisionmaking process. It has been suggested that LPs performed prior to 12 hours from onset of symptoms may give false-negative results either because blood has not

\*See definitions of emergent and urgent under Background, question III.

diffused down or because sufficient time has not elapsed to allow for xanthochromia to appear.<sup>38</sup>

In 1986, Day and Raskin<sup>39</sup> described a 42-year-old woman who presented with 3 thunderclap headaches within 1 week. The patient was evaluated for an SAH with negative findings in both a CT scan and bloodless CSF at 12 hours after the first attack and 10 hours after the last attack. Because the character of the patient's headaches was worrisome, angiography was performed. The angiogram showed diffuse marked vasospasm and an unruptured aneurysm. It was concluded that either hemorrhage into the wall of the aneurysm or rapid expansion of the aneurysm could have been the cause of the patient's headaches. This case report raised the prospect that normal findings in both a CT scan and LP are not enough to exclude an aneurysmal cause of thunderclap headache.

**Findings.** There are no well-designed, prospective cohort studies to support or refute the need for angiography in patients with thunderclap headache and negative findings in both a CT scan and LP. Wijndicks et al<sup>40</sup> conducted a follow-up study during a 3.3-year period on 71 patients, each of whom presented with a thunderclap headache with negative findings for SAH in both a CT scan and LP. Angiograms were performed on 6 of 71 patients, all of which revealed negative findings. None of these patients suffered from SAH during the 3.3-year follow-up period. Seventeen percent had identical recurrences of their headaches; 44% developed tension headaches or migraines without aura. Based on their findings, the authors concluded that angiography is not recommended for the workup of these patients. In addition, Wijndicks et al suggested that the patient described by Day and Raskin<sup>39</sup> had experienced the thunderclap headache as a result of the diffuse vasospasm seen on the angiogram and that the aneurysm found was merely an incidental finding. Case reports by Slivka and Phibrook<sup>41</sup> and Dodick et al<sup>42</sup> described a total of 6 patients with thunderclap headache in the absence of SAH. Angiography on all of these patients revealed multifocal segmental vasospasm without aneurysm. These papers demonstrate that vasospasm is certainly one cause of thunderclap headache.

In a prospective study on 49 patients with thunderclap headache, Harling et al<sup>26</sup> found similar results to Wijndicks et al.<sup>40</sup> Fourteen of 49 patients presenting with a thunderclap headache had negative findings on both a CT scan and LP. These patients were followed up for a minimum of 18 months, and none suffered from SAH. Although this is a prospective study refuting the need for angiography in the initial workup of thunderclap headache, it is flawed by its low study power caused by its limited sample size.

Raps et al<sup>43</sup> looked at the clinical spectrum of unruptured intracranial aneurysms through a retrospective study on 111 patients. Fifty-four patients had symptomatic aneurysms. The authors documented 8 clinical syndromes of symptomatic unruptured aneurysms. An acute headache such as a thunderclap headache was described in 7 patients. Based on their postsurgical evaluation of the aneurysm, Raps et al proposed an aneurysmal mechanism of thunderclap headache, which included aneurysmal expansion, thrombosis, and intramural hemorrhage.

In 1992, Hughes<sup>44</sup> presented 2 case reports of patients presenting with thunderclap headaches of a prolonged nature. Workup in these patients revealed negative findings for SAH; however, angiograms done approximately 2 weeks later revealed 5-mm aneurysms. Hughes argued that although the yield of angiography in these cases of thunderclap headache is low, angiography needs to remain a part of the workup because of the high morbidity and mortality associated with the disease. Of note, the prevalence of inconsequential intracranial aneurysms found at autopsy is between 2% and 5%.<sup>45</sup> Thus, the aneurysms found in Hughes' case report could have been an incidental finding. It is also possible that, at the time these patients presented with their thunderclap headaches, vasospasm was present, but by the time the angiograms were obtained 2 weeks later, when the headaches had resolved, the vasospasm had also resolved.

An SAH is not the only condition that can present with a thunderclap headache. A number of strength of evidence Class III studies demonstrate that a group of patients with cerebral venous thrombosis can present with an acute severe headache without neurologic deficits.<sup>46-48</sup> Often, these patients present with normal findings in a head CT scan, but, although there may be no blood or xanthochromia in the CSF, the opening pressure on the LP may be elevated.

In a retrospective study of all patients seen at the Mayo Clinic with a diagnosis of internal carotid artery dissection or vertebral artery dissection, 13 of 92 patients with headache and internal carotid artery dissection and 14 of 18 patients with vertebral artery dissection described their headache as sudden and severe.<sup>49</sup>

#### **Patient management recommendations.**

**Level A recommendations.** None specified.

**Level B recommendations.** None specified.

**Level C recommendations.** Patients with a thunderclap headache who have negative findings in a head CT scan, normal opening pressure, and negative findings in CSF

analysis do not need emergent angiography and can be discharged from the ED with follow-up arranged with their primary care provider or neurologist.

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**Evidentiary Table.**

*Treatment.*

<b>Study</b>	<b>Design</b>	<b>Findings</b>	<b>Limitations</b>	<b>Conclusions</b>	<b>Grade</b>
Seymour et al <sup>9</sup>	Case series	3 patients with intracranial hemorrhages presenting with headache who responded to either ketorolac or prochlorpromazine.	Design		III
Gross et al <sup>10</sup>	Case series	3 patients with headache from inflammatory processes (infections or carcinomatous meningitis) who responded to dihydroergotamine or metoclopramide.	Design		III
Lipton et al <sup>11</sup>	Case report	1 patient with headache from carbon monoxide poisoning who responded to sumatriptan.	Design		III

**Evidentiary Table.**  
*Lumbar puncture.*

Study	Design	Findings	Limitations	Conclusions	Grade
Duffy <sup>16</sup>	It is unclear whether this is a retrospective study or a 2-year prospective observational study. Inclusion: patients considered to have a complication caused by the LP had to have clinical deterioration while the spinal needle was still in place. Exclusion: Patients whose clinical status changed after the LP was performed.	74 patients included in analysis. 44 had LP before CT scan. 7 of the 44 patients deteriorated while LP was being performed. All were drowsy, confused, or had "mild" hemiparesis before performing the procedure. 6 of the 7 patients had structural evidence of herniation in the operating room or at autopsy. 4 of the 7 died and 3 of the 7 had long-term neurologic sequelae. 12 patients had hemispheric shift on CT scan, 5 underwent LP, and 3 of the 5 deteriorated subsequent to LP.	Unclear study design. There was no standardization in the management of these patients. LP in patients with no neurologic signs were not included.	The risk of herniation is significant in patients who undergo spinal tap and have an intracranial hematoma with a hemispheric shift.	III
French and Glasgow <sup>17</sup>	Retrospective chart review of 109 patients admitted for SAH. Inclusion: Patients who were drowsy, confused, or had "mild" hemiparesis. Exclusion: Stupor, coma, or "significant" hemiparesis.	27 excluded because of severe neurologic deficits. 70 of 82 had an LP, and none deteriorated immediately. 14 of the 82 had an intracranial hematoma (4 without localizing signs); 7 of the 14 had LP without sequelae.	Retrospective study design. Timing of CT scans was not reported. No long-term outcome data reported.	Herniation, even in the neurologically symptomatic patient, is uncommon.	III
Zisfein and Tuchman <sup>18</sup>	Prospective observational design during a 3-year period. Inclusion: Patients requiring an LP to rule out meningitis who subsequent to procedure, are found within 1 week to have a space-occupying lesion by CT scan. Exclusion: Patients in whom an LP is done but no intracranial mass lesion is documented by CT scan.	38 patients were included. 34 of the 38 patients' CT scans revealed mass effect. The 4 remaining studies were of poor quality and could not be evaluated for this finding. 37 of the 38 patients were the same or improved 48 hours after the LP. One patient with fixed dilated pupils and absent corneal reflexes before the LP subsequently died. 3 patients who were worsening before the LP continued to do poorly but returned to baseline.	Indications for suspicion of meningitis are not reported. Without a pre-spinal tap CT scan there is no way to know whether the shift on CT scan resulted from the LP. No patients suspect for SAH are included. Heterogeneous group of CNS lesions.	Herniation is uncommon in the setting of intracranial mass lesions even in the presence of mass effect.	III
Gopol et al <sup>19</sup>	Consecutive patient assessments during an 18-month period. Preselected history and physical examination data were collected on all patients who were determined to need an LP. The senior emergency physician's suspicion that a patient would have a CT finding that would contraindicate LP was also documented before performing the CT scan.	111 patients were assessed. Reasons for LP: rule out SAH (42.3%), rule out meningitis (36.9%), and other (20.7%). 15.3% (15) had documented lesions. 2.7% (3) had contraindications to LP (a lesion with mass effect). Physicians were able to predict all patients who were found to have contraindications to LP. Altered mental status, papilledema, and focal neurologic examination increased the likelihood of an abnormal CT finding. Absence of historical or physical findings had a negative likelihood ratio of 0 for finding new CNS pathology.	Heterogeneous patient population. Small number of patients with disease.	Supports the notion that patients without focal neurologic findings, signs of increased intracranial pressure, or altered mental status are unlikely to have radiologic findings that contraindicate LP.	II

**Evidentiary Table.**  
*Neuroimaging.*

Study	Design	Findings	Limitations	Conclusions	Grade
Dhopes et al <sup>20</sup>	1-year retrospective review.	872 patients, 2.5% of ED visits; 25% pediatrics. 65% primary complaint. 4.7% admitted. 8 patients with intracranial hemorrhage; 5 with meningitis, 2 with subdurals, 1 with tumor.	In this study, 1% of ED patients had a significant intracranial process causing their headache, but diagnostic testing and follow-up is not clearly presented.	Study does not present enough information to assist in decisionmaking.	III
American Academy of Neurology <sup>23</sup>	Literature review by the AAN. 17 studies in the evidentiary table. Inclusion: Patients with normal findings in a neurologic examination.	Analysis of literature on chronic migraine demonstrates low yield of neuroimaging when neurologic examination findings are normal. No data for acute onset of new headache. Attempts to analyze impact on outcome of early asymptomatic lesions (eg, arteriovenous malformations, tumors) before onset of neurologic symptoms.		"In patients with atypical headache patterns, a history of seizures, or focal neurologic signs or symptoms, CT or MRI may be indicated."	III
Lledo et al <sup>25</sup>	1-year prospective study. Inclusion: Acute sudden-onset headache with no past history, normal findings in a neurologic examination by neurologist. All patients had CT, if the results of the CT were normal, an LP was done. 3-month follow-up.	27 patients enrolled: 9 with SAH, 1 with intraventricular hemorrhage, 1 with bacterial meningitis, 1 with viral meningitis, 15 unknown. No combination of findings identified the patients with SAH. CT findings were positive in only 4 of 9 patients with SAH.	No exclusion criteria given. Small sample with no power analysis. Patients only followed up for 3 months; no angiograms were performed to rule out unruptured aneurysm.	Neither altered mental status, neurologic examination, nor improving symptoms distinguished the group with SAH.	I
Harling et al <sup>26</sup>	Prospective study. 49 patients with sudden headache suggestive of SAH. 14 had negative findings on CT/LP. Patients were followed up at 18 months.	35 of the 49 patients had positive findings on CT or LP for SAH. Unable to distinguish on clinical grounds those with or without SAH. 8 of the 14 with normal findings on CT/LP had angiogram; all revealed normal findings. At 18 month follow-up, no adverse outcomes.	Selection bias. Small numbers. Inclusion criteria not defined. Not all patients had angiogram.	Angiogram is not indicated in patients with thunderclap headache who have negative findings on CT/LP.	II
Mitchell et al <sup>27</sup>	Prospective study: consecutive patients from military ED and clinics. Inclusion: Headache of undetermined etiology. Exclusion: seizures, trauma, neoplasms, known etiology of headache.	350 patients. 7 (2%) had significant findings (eg, tumor, subdural, SAH, hydrocephalus, sinusitis). 27 patients had abnormal examination results but normal CT results. All patients with positive findings on CT had abnormal physical or neurologic examination results or unusual clinical symptomatology ("worst headache," hypersomnolence, feeling of going crazy, positional headache, headache waking from sleep). 27 reported "worst headache of life"; only 1 SAH. Unusual symptomatology ("worst headache," syncope, vomiting, etc.) did not predict positive findings on scans.	Study done by radiology; no protocol for referral. Although consecutive patients were referred from ED and clinics, it does not necessarily represent consecutive patients who presented to ED or clinics with headache; therefore, selection bias.	Historical or physical abnormalities are not sensitive for intracranial process, but abnormal physical or historical findings increase the likelihood of positive CT findings.	II
Mills et al <sup>28</sup>	Prospective observational study of patients receiving an urgent CT scan from the ED.	42 patients in the headache subset (407 patients total); 21% had positive CT findings. Only 1 patient with a focal examination. 29% with "worst headache of life" had positive CT findings (LP results not provided).	Enrollment dependent on house-staff; selection bias. Neurologic examination by emergency medicine housestaff. Trauma patients included but percent not available.		III
Akpek et al <sup>29</sup>	Retrospective study. Inclusion: No neurologic findings. Exclusion: Complaints of vision change, vertigo, dizziness, personality change, cancer.	592 patients between the ages of 8 and 88 years. No patients with acute intracranial processes were identified.	This was a retrospective study. No formal neurologic examinations were reported; all of the exclusion criteria were not reported, but appears to be extremely strict.	Study supports observation in patients with normal findings in a neurologic examination and without a history of vision change, vertigo, dizziness, personality change, or cancer. Emphasizes importance of careful history.	II

**Evidentiary Table. (continued)**

*Neuroimaging.*

Study	Design	Findings	Limitations	Conclusions	Grade
Demaerel et al <sup>30</sup>	363 consecutive patients with chronic headache referred to radiology for CT with and without contrast. Inclusion: Normal neurologic examination findings. Exclusion: Vertigo, dizziness, migraine, epilepsy.	11 (3%) had a space-occupying lesion; none needed emergent surgery.	Did not look specifically at acute headache. Selection bias in that group of patients who were chosen from a larger pool for neuroimaging.	Supports referral of patients with chronic headache with normal neurologic examination findings for neurology follow-up; does not support obtaining an emergent CT in these patients.	III
Ramirez-Lassepas et al <sup>31</sup>	Retrospective review during a 15-month period of patients with complaint of headache; random selection of 329 charts of 1,720 patients and of 139 hospitalized patients. Follow-up at 6 months.	4.5% of patients seen in the ED were evaluated for headache (1,859/44,080). 139 (6.9%) were hospitalized. 3.8% of patients had an intracranial process (SAH, tumor, intracranial hemorrhage, bacterial meningitis, cerebral infarction, herpes encephalitis). No association found between type of headache and pathologic entities. Abnormal neurologic examination findings and headache had a 39% positive predictive value for intracranial process. Acute onset, occipitotonal location, and age >55 years were identified as clinical parameters associated with intracranial process.	Selection process and inclusion or exclusion criteria were not well described No follow-up of patient discharged from the ED. Randomization process not described. Hospitalized patients not described.	Clinical findings and historical findings had a low positive predictive value but absence had a high negative predictive value.	II
Kahn et al <sup>32</sup>	Retrospective; 2 centers, United States versus Canada. Inclusion: Acute migraine or headache. Exclusion: Trauma or surgery.	1,111 examinations during a 3-year period; 11% had an acute intracranial process, (eg, hemorrhage, infarction, tumor); 18% had chronic processes (eg, old infarction, atrophy). Frequency highest in hospitalized patients and those >40 years. Proportion of positive findings in the migraine group did not differ from other groups.	Did not provide clinical information that directed testing; mentions that only 155 examinations were done for headache alone, implying positive physical findings but not actually providing them.	Study does not specifically address predictors of positive findings because the population studied is not well described.	III
Duarte et al <sup>33</sup>	Prospective study of 100 consecutive patients with new headache first occurring within 1 year of presentation. Patients recruited from general practitioners. All patients had CT with and without contrast. All patients older than 60 years had erythrocyte sedimentation rate.	80 patients had normal examination findings. 21 had intracranial neoplasms (13 with normal neurologic examination findings). No combination of historical or physical findings excluded headache patients with intracranial process; however, no patient needed emergent neurosurgery.	Recruitment procedures biased referral; therefore, population did not necessarily reflect ED population. Does not deal specifically with acute headache.	Although the study identified a large number of patients with intracranial process, it failed to identify those patients in need of an imaging study in the ED.	II
Reinus et al <sup>34</sup>	Retrospective review of consecutive ED patients complaining of acute headache or acutely worsened headache who underwent CT.	333 patients; 33 (10%) had positive CT findings. 76 (23%) had positive neurologic examination findings (focal deficit or altered mental status); patients with positive examination findings were 11 times more likely to have positive CT results. 17 had "worst headache of their life"; only 1 had positive CT results. Combination of normal neurologic examination findings, no altered mental status, no amnesia, and no hypertension had a 98% negative predictive value.	Study methods do not state how many patients with acute headache did not have a CT scan performed. 25% of study population were trauma patients. Retrospective design did not ensure that historical or neurologic findings were identified.	Study supports the importance of a neurologic examination; however, 29 of 34 patients with focal findings did not have positive CT findings, and 4% of patients with normal neurologic examination findings had positive CT results. Although only 1 of 17 patients with the "worst headache of their life" had positive CT results, LP was not reported.	II

**Evidentiary Table. (continued)***Neuroimaging.*

<b>Study</b>	<b>Design</b>	<b>Findings</b>	<b>Limitations</b>	<b>Conclusions</b>	<b>Grade</b>
Lipton et al <sup>35</sup>	Prospective study of 49 consecutive HIV-positive patients with headache.	40 (82%) had a serious identifiable cause. 39% had cryptococcal meningitis; 16% had toxoplasmosis; 35% had mass lesions.	Entry criteria do not specify CD4 count or whether headache was new onset. Mass lesions were not characterized.	Study supports taking an HIV risk-factor history in patients with headache and obtaining CT/LP in HIV-positive patients with headache.	II
Rothman et al <sup>36</sup>	Prospective convenience sample. Inclusion: New or changed neurologic examination. Standardized neurologic examination.	110 patients: 24% had focal lesions, and 18% were new lesions, of which 7% had mass effect. New seizure, changed mental status, or headache different in quality or lasting more than 3 days would have identified all patients with a new focal CNS lesion. New or different headache was reported in 25% of patients. 76% of patients with a new lesion required emergent management.	Study included all neurologic complaints, not just headache. Convenience sample.		II
de Bruijn et al <sup>46</sup>	Case series of 10 patients (subset of 71 patients with cerebral venous sinus thrombosis in a randomized study).	Of the patients who presented with thunderclap headache, 5 had negative CT findings and 5 had misinterpreted CT findings. Diagnosis of cerebral venous sinus thrombosis was made with MRI or angiography.	Not all patients received the same evaluation, (eg, only 1 had an LP).	Study supports close follow-up for patients with thunderclap headache and the need to consider angiogram.	III

**Evidentiary Table.**

*Thunderclap headache.*

Study	Design	Findings	Limitations	Conclusions	Grade
Harling et al <sup>26</sup>	Prospective study. 49 patients with sudden headache suggestive of SAH. 14 had negative findings on CT/LP. Patients were followed up at 18 months.	35 of the 49 had positive findings on CT or LP for SAH. Unable to distinguish on clinical grounds those with or without SAH. 8 of the 14 with normal CT/LP findings had angiogram; all revealed normal results. At 18-month follow-up, no adverse outcomes.	Selection bias. Small numbers. Inclusion criteria not defined. Not all patients had angiogram.	Angiogram is not indicated in patients with thunderclap headache who have negative CT/LP findings.	II
Day and Raskin <sup>39</sup>	Case report.	Negative CT/LP findings.	Design		III
Wijdicks et al <sup>40</sup>	Prospective (follow-up) study.	71 patients with thunderclap headache who had negative CT/LP findings. Follow-up for an average of 3.3 years. 6 patients had angiograms: all revealed normal findings. 17% had identical recurrence; no negative outcomes.	Not all patients had the same diagnostic evaluation, and only 6 of the 71 had an angiogram.	Authors conclude that patients with negative CT/LP findings can be safely discharged without further study.	II
Slivka and Philbrook <sup>41</sup>	Case report: 4 cases.	4 patients with thunderclap headache who had angiograms that demonstrated vasospasm but no aneurysm. All headaches resolved spontaneously.	Design	Vasospasms alone can cause thunderclap headache. Authors propose a separate classification for this type of headache.	III
Dodick et al <sup>42</sup>	Case report: 2 cases.	Reversible intracranial vasospasm without aneurysm. Benign outcome.	Design		III
Raps et al <sup>43</sup>	Retrospective study of patients presenting to a tertiary care center with unruptured intracranial aneurysm. Histories, operative reports, and angiograms of 111 patients reviewed.	54 of 111 patients had acute symptoms; 7 presented with a thunderclap headache; all had at least transient neurologic deficits.	Diagnostic protocol is not described. Results of CT and LP are not provided. Selection bias.	Article supports that patients with unruptured SAH can present with a thunderclap headache and suggests the benefit of pursuing a diagnosis with angiography.	III
Hughes <sup>44</sup>	Case report; 2 cases.	CT findings were negative; 1 had LP findings that were negative. Aneurysms on angiogram without evidence of vasospasm.	Design		III
de Bruijn et al <sup>46</sup>	Case series of 10 patients (subset of 71 patients with cerebral venous sinus thrombosis in a randomized study).	Of patients who presented with thunderclap headache, 5 had negative findings on CT and 5 had misinterpreted findings on CT. Diagnosis of cerebral venous sinus thrombosis was made with MRI or angiography.	Not all patients received the same evaluation, (eg, only 1 had an LP).	Study supports close follow-up for patients with thunderclap headache and need to consider angiogram in such patients.	III
Daif et al <sup>47</sup>	Retrospective chart review.	35% of patients had acute-onset headache; 82% had onset with headache; 80% had papilledema; 10% had seizures; and 30% had focal neurologic deficit. 17 of 40 patients had normal findings on CT. 18 of 19 patients had diagnostic MRI. 29 of 31 patients demonstrated increased intracranial process on LP.	Not all patients received the same diagnostic workup.	Many of the patients presented as idiopathic intracranial hypertension patients.	III
Boussier et al <sup>48</sup>	Retrospective case series.	Of 38 patients, 74% had headache; 34% had focal findings; and 5 had normal CT findings.	Not all patients received the same diagnostic workup.	4 patients died, emphasizing the importance of making the diagnosis. Many patients were initially thought to have idiopathic intracranial hypertension.	III