

**American College of Emergency Physicians**

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

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**From the American College of Emergency Physicians Clinical Policies Subcommittee (Writing Committee)  
on Critical Issues in the Evaluation and Management of Adult Patients Presenting to the ED with Acute  
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56

57 **ABSTRACT**

58

59 This clinical policy from the American College of Emergency Physicians is an update of a 2002 clinical  
60 policy on the evaluation and management of adult patients presenting to the emergency department (ED) with  
61 acute, nontraumatic headache. A writing subcommittee reviewed the literature to derive evidence-based  
62 recommendations to help clinicians answer the following 5 critical questions: (1) Does a response to therapy  
63 predict the etiology of an acute headache? (2) Which patients with headache require neuroimaging in the ED?  
64 (3) Does lumbar puncture need to be routinely performed on ED patients being worked up for nontraumatic  
65 subarachnoid hemorrhage whose noncontrast brain computed tomography (CT) scans are interpreted as normal?  
66 (4) In which adult patients with a complaint of headache can a lumbar puncture be safely performed without a  
67 neuroimaging study? (5) Is there a need for further emergent diagnostic imaging in the patient with sudden-onset,  
68 severe headache who has negative findings in both CT and lumbar puncture? Evidence was graded and  
69 recommendations were given based on the strength of the available data in the medical literature.

70

71 **INTRODUCTION**

72 A query of the National Hospital Ambulatory Medical Care Survey for 1999 to 2001 found that headache  
73 accounted for 2.1 million emergency department (ED) visits (2.2 % of all ED visits). Of the 14% of the patients  
74 who underwent imaging, 5.5% received a pathologic diagnosis.<sup>1</sup> Emergency physicians must determine which  
75 patients need neuroimaging in the ED and which can be appropriately deferred and evaluated in the outpatient  
76 setting. Many patients have limited access to care, which further complicates this decision process in clinical  
77 practice, but this variable is not accounted for in most studies. When evaluating the data, the outcome measures  
78 used in determining the need for neuroimaging in the ED must also be clinically relevant to practice. For example,  
79 diagnosing a brain tumor may not require immediate neurosurgery or even hospitalization, yet may clearly direct  
80 the disposition and follow-up timing of the patient. This policy is an update of the 2002 American College of  
81 Emergency Physicians (ACEP) clinical policy on headache.<sup>2</sup>

82 In deciding which test to perform, emergency physicians must assess pretest risk for the condition.  
83 Researchers in Ottawa, Ontario, conducting an observational study in patients with severe headache, asked  
84 emergency physicians to rate their comfort level in performing a lumbar puncture without first obtaining a head  
85 computed tomography (CT) scan, as well as their estimates of pretest probability of a subarachnoid hemorrhage in  
86 these patients.<sup>3</sup> Of the 1,070 eligible patients, 747 were prospectively enrolled, with 50 patients having a  
87 confirmed subarachnoid hemorrhage. Emergency physicians were either “uncomfortable” or “very  
88 uncomfortable” with performing a lumbar puncture without a head CT scan in 49.6% of 625 patients. They were  
89 “very comfortable” with performing a lumbar puncture with a head CT scan in only 10.2% of patients with acute  
90 headache. Emergency physicians were better at identifying patients at low risk for subarachnoid hemorrhage and  
91 less accurate at identifying the high-risk patients. Emergency physicians’ estimate of the probability of the patient

92 having a subarachnoid hemorrhage revealed a receiver operating characteristic curve with an area of 0.85 (95%  
93 confidence interval [CI] 0.80 to 0.91). The sensitivity of clinical suspicion was 93% (95% CI 81% to 97%) and  
94 specificity was 49% (95% CI 45% to 53%) using a pretest probability of 2% or greater as the threshold.  
95 Researchers believed that emergency physicians discriminate moderately well between headache due to  
96 subarachnoid hemorrhage and other causes. However, given the high mortality associated with a missed  
97 diagnosis, emergency physicians are currently unwilling to trust their judgment. There were 3 subarachnoid  
98 hemorrhage cases in which pretest probability was 2% or lower, which may explain why many emergency  
99 physicians continue to use diagnostic tests on patients with low pretest probability.<sup>3</sup>

100

## 101 **METHODOLOGY**

102

103 This clinical policy was created after careful review and critical analysis of the medical literature.

104 Multiple searches of MEDLINE and the Cochrane database were performed. Specific key words/phrases used in  
105 the searches are identified under each critical question. To update the 2002 ACEP policy, which used literature up  
106 to December 1999, all searches were limited to English-language sources, human studies, adults, and years  
107 January 2000 to August 2006. Additional articles were reviewed from the bibliography of articles cited and from  
108 published textbooks and review articles. Subcommittee members supplied articles from their own files, and more  
109 recent articles identified during the expert review process were also included.

110 The reasons for developing clinical policies in emergency medicine and the approaches used in their  
111 development have been enumerated.<sup>4</sup> This policy is a product of the ACEP clinical policy development process,  
112 including expert review, and is based on the existing literature; when literature was not available, consensus of  
113 emergency physicians was used. Expert review comments were received from individual emergency physicians  
114 and from individual members of the American Association of Neurological Surgeons/Congress of Neurological  
115 Surgeons, the American Headache Society, and the Society for Academic Medicine. Their responses were used to  
116 further refine and enhance this policy; however, their responses do not imply endorsement of this clinical policy.  
117 Clinical policies are scheduled for revision every 3 years; however, interim reviews are conducted when  
118 technology or the practice environment changes significantly.

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121

122  
123 All articles used in the formulation of this clinical policy were graded by at least 2 subcommittee  
124 members for strength of evidence and classified by the subcommittee members into 3 classes of evidence on the  
125 basis of the design of the study, with design 1 representing the strongest evidence and design 3 representing the  
126 weakest evidence for therapeutic, diagnostic, and prognostic clinical reports, respectively (Appendix A). Articles  
127 were then graded on 6 dimensions thought to be most relevant to the development of a clinical guideline: blinded  
128 versus nonblinded outcome assessment, blinded or randomized allocation, direct or indirect outcome measures  
129 (reliability and validity), biases (eg, selection, detection, transfer), external validity (ie, generalizability), and  
130 sufficient sample size. Articles received a final grade (Class I, II, III) on the basis of a predetermined formula,  
131 taking into account design and quality of study (Appendix B). Articles with fatal flaws were given an “X” grade  
132 and not used in formulating recommendations in this policy. Evidence grading was done with respect to the  
133 specific data being extracted and the specific critical question being reviewed. Thus, the level of evidence for any  
134 one study may vary according to the question, and it is possible for a single article to receive different levels of  
135 grading as different critical questions are answered. Question-specific level of evidence grading may be found in  
136 the Evidentiary Table included at the end of this policy.

137 Clinical findings and strength of recommendations regarding patient management were then made  
138 according to the following criteria:

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

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

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

148

149

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

154           This policy is not intended to be a complete manual on the evaluation and management of adult patients  
155 with acute headache but rather a focused examination of critical issues that have particular relevance to the  
156 current practice of emergency medicine.

157           It is the goal of the Clinical Policies Committee to provide an evidence-based recommendation when the  
158 medical literature provides enough quality information to answer a critical question. When the medical literature  
159 does not contain enough quality information to answer a critical question, the members of the Clinical Policies  
160 Committee believe that it is equally important to alert emergency physicians to this fact.

161           Recommendations offered in this policy are not intended to represent the only diagnostic and  
162 management options that the emergency physician should consider. ACEP clearly recognizes the importance of  
163 the individual physician's judgment. Rather, this guideline defines for the physician those strategies for which  
164 medical literature exists to provide support for answers to the crucial questions addressed in this policy.

165           *Scope of Application.* This guideline is intended for physicians working in hospital-based EDs.

166

167           *Inclusion Criteria.* This guideline is intended for adult patients presenting to the ED with acute,  
168 nontraumatic headache.

169

170           *Exclusion Criteria.* This guideline is not intended to address the care of pediatric patients or the care of  
171 patients with trauma-related headaches.

172

## 173 **CRITICAL QUESTIONS**

### 174 **1. Does a response to therapy predict the etiology of an acute headache?**

#### 175 **Patient Management Recommendations**

176           *Level A recommendations.* None specified.

177           *Level B recommendations.* None specified.

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

180

181           Key words/phrases for literature searches: thunderclap headache, acute headache, response to therapy,  
182 cause or etiology, and variations and combinations of the key words/phrases.

183  
184           Because headache is a common complaint, physicians have sought ways to differentiate the serious life-,  
185 limb-, vision-, or brain-threatening etiologies from the more benign ones. Defining who can be sent home safely  
186 without work-up beyond medical history and physical examination could expedite patient care while decreasing  
187 patient cost. Anecdotally, some clinicians have tried to use a favorable response to medications as an indicator  
188 that a patient’s headache is not due to a secondary (serious) etiology. To fully address this question, it is important  
189 to understand the underlying pathophysiology of headache and the pharmacologic rationale behind the current  
190 concepts in therapy.

191           Current understanding of headache suggests that there is a common pathway for the pain regardless of the  
192 underlying etiology. Much of our understanding about the pathophysiologic characteristics comes from research  
193 on migraine. In essence, headache can be caused by (1) distention, traction, or dilation of intracranial or  
194 extracranial arteries; (2) traction or displacement of large intracranial veins or the dural envelope; (3)  
195 compression, traction, or inflammation of cranial and spinal nerves; (4) head and neck muscle spasm,  
196 inflammation, or trauma; (5) meningeal irritation; (6) raised intracranial pressure; and (7) disturbance of  
197 intracerebral serotonergic projections.<sup>5</sup>

198           Evidence suggests that headache pain is transmitted by the trigeminal nerve from the blood vessels of the  
199 pia mater and dura mater.<sup>6</sup> The exact trigger of the pain may be multifactorial, but once the trigger occurs, the  
200 trigeminovascular axons are stimulated, resulting in the onset of pain and release of neurogenic peptides stored in  
201 the afferent C fibers innervating cephalic blood vessels. These vasoactive neuropeptides then stimulate endothelial  
202 cells, mast cells, and platelets, creating an inflammatory cascade known as “neurogenic inflammation.”  
203 Vasodilatation with enhanced permeability of plasma proteins follows with a perivascular inflammatory reaction.<sup>7</sup>  
204 “Neurogenic inflammation” within the cephalic tissue is one model that has been proposed as the pathogenic  
205 mechanism of headache. However, selective and potent inhibitors of “neurogenic inflammation” have thus far  
206 proven ineffective in clinical trials.

207           Serotonin (5-HT) receptors are the main focus of pain management because they are known to modulate  
208 neurogenic peptide release and vasoconstrict dilated dural vessels.<sup>8</sup> The goal of therapy is to prevent or abort the  
209 neurogenic inflammation that occurs as a result of neuropeptide release. Subtypes of the 5-HT<sub>1</sub> receptor are  
210 believed to be the most important receptors in the final common pathway of headache. Despite many adverse

211  
212 effects, 5-HT is a potent vasoconstrictor, a property that may be a factor in its ability to treat migraines.  
213 Pharmacologic agents with an affinity for 5-HT receptors are currently the preferred therapy in acute headache  
214 management. Some agents, such as the triptans, are specific agonists at the 5-HT<sub>1</sub> receptor, whereas other  
215 medications, such as dihydroergotamine, prochlorperazine, and metoclopramide, act at a variety of 5-HT and  
216 other aminergic receptors.<sup>5,9</sup>

217       There are no prospective randomized controlled trials, evidence from meta-analysis from randomized  
218 controlled trials, or well-designed cohort studies to support or refute the practice of using response to therapy in  
219 nontraumatic headaches as an indicator of potential underlying pathologic entities. The only published data about  
220 response to pain medications as an indicator of underlying headache etiology is in Class III evidence in the form  
221 of case reports and case series.

222       Numerous articles have described headaches of varying secondary (serious) etiologies showing clinical  
223 improvement or resolution of pain in response to many different analgesics. These conditions include but are not  
224 limited to the following: intracerebral hemorrhage/subarachnoid hemorrhage (ibuprofen, ketorolac,  
225 prochlorperazine),<sup>10</sup> viral meningitis/meningeal carcinomatosis (dihydroergotamine and metoclopramide),<sup>11</sup>  
226 carbon monoxide–induced headache (sumatriptan),<sup>12</sup> cerebral venous thrombosis (sumatriptan and various  
227 common analgesics),<sup>13</sup> carotid artery dissection (sumatriptan),<sup>14,15</sup> subarachnoid hemorrhage (sumatriptan),<sup>16,17</sup>  
228 and cysts of the cavum septi pellucidi (indomethacin).<sup>18</sup>

## 229 **2. Which patients with headache require neuroimaging in the ED?**

### 230 **Patient Management Recommendations**

231       *Level A recommendations.* None specified.

232       *Level B recommendations.*

233       1. Patients presenting to the ED with headache and new abnormal findings in a neurologic  
234 examination (eg, focal deficit, altered mental status, altered cognitive function) should undergo emergent\*  
235 noncontrast head CT.

236       2. Patients presenting with new sudden-onset severe headache should undergo an emergent\* head CT.

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

239       *Level C recommendations.* Patients who are older than 50 years and presenting with new type of  
240 headache but with a normal neurologic examination should be considered for an urgent<sup>†</sup> neuroimaging study.

241  
242 \**Emergent studies* are those essential for a timely decision regarding potentially life-threatening or severely  
243 disabling entities. <sup>†</sup>*Urgent studies* are those that are arranged prior to discharge from the ED (scan appointment is

244 included in the disposition) or performed prior to disposition when follow-up cannot be assured. *Routine studies*  
245 are indicated when the study is not considered necessary to make a disposition in the ED.<sup>19</sup>

246  
247 Key words/phrases for literature searches: acute headache, diagnostic imaging, CT scan, MRI, emergency  
248 department, and variations and combinations of the key words/phrases.

249 The primary focus in obtaining a neuroimaging study in the ED is to identify a treatable lesion. Treatable  
251 lesions include tumors, vascular malformations, aneurysms, subarachnoid hemorrhage, cerebral venous sinus  
252 thrombosis, subdural and epidural hematomas, infections, stroke, hydrocephalus, and others. These positive  
253 findings may provide tangible outcomes that can be clearly assessed from a clinical and financial perspective.  
254 Less tangible is the impact of reassurance to the patient who has a normal study result. In one study, 60% of  
255 patients presenting with headache to an outpatient neurology clinic had concerns of harboring significant  
256 pathologic findings, and 40% of those reassured that they had no reason for concern left questioning their  
257 evaluation.<sup>20</sup>

258 The need for neuroimaging in headache patients has been addressed in 5 previous guidelines.<sup>2,9,21-23</sup>  
259 Although some of their recommendations are relevant to the acute setting, 3 of them focus more on patients with  
260 chronic headache in the primary care setting.<sup>9,21,22</sup> In addition to noncontrast head CT scan, contrast brain CT, CT  
261 angiography, and magnetic resonance imaging (MRI) may also be useful, depending on the differential diagnosis  
262 and other characteristics of the individual patient.

263 The cornerstone to assessing the patient with a headache is the medical history and physical examination.  
264 Although this seems obvious, it is worth emphasizing because no decisionmaking can take place without  
265 appropriate data. There exists significant variation in the literature as to what are important historical and clinical  
266 markers. There is also considerable contradiction in the literature about the positive predictive value of specific  
267 findings.<sup>21,24-29</sup> An abnormal finding on neurologic examination is frequently cited as an indication for emergent  
268 neuroimaging. In a Class II study, Ramirez-Lassepas et al<sup>30</sup> retrospectively reviewed the records of 468 patients  
269 who presented to the ED with a chief complaint of headache. The authors reported that abnormal findings in a  
270 neurologic examination had a positive predictive value of 39% for intracranial pathology. The US Headache  
271 Consortium,<sup>22</sup> in their review of articles dealing with chronic headache, calculated likelihood ratios (LRs) for  
272 patients presenting with headache and focal neurologic findings. They reported that the presence of an  
273 abnormality on the neurologic examination increased the likelihood of positive results 3-fold (95% CI 2.3 to 4.0)

274  
275 in a neuroimaging study. Normal findings in a neurologic examination reduced the odds of positive findings in a  
276 neuroimaging study by 30%.

277         Historical findings that have prompted neuroimaging in headache patients include older age.<sup>30-32</sup> These  
278 various studies used different age cut-offs in the range of 50 years to 60 years, and it is important to recognize that  
279 age is not a dichotomous variable. Adding to this literature, a multivariate analysis of the results from the 1999 to  
280 2001 National Hospital Ambulatory Medical Care Survey for headache on all available historical factors revealed  
281 that patients over 50 years of age were more likely to receive a pathologic diagnosis (odds ratio [OR] 3.3, CI 1.2  
282 to 9.3).<sup>1</sup> No additional risk factors were identified from this latter study. Other historical findings for initiation of  
283 neuroimaging include occipital location of pain,<sup>30</sup> worsening of headache with Valsalva,<sup>32</sup> headache waking  
284 patient from sleep,<sup>28,32</sup> and headache associated with syncope, nausea, or sensory distortion.<sup>28</sup> The Headache  
285 Consortium calculated likelihood ratios for each of these symptoms and, based on the best available evidence in  
286 the literature, found that these symptoms may increase the probability of positive findings in a neuroimaging  
287 study but reported that the CIs are so wide that clear recommendations could not be made.<sup>22</sup>

288         Three subsets of headache patients deserve special mention: those presenting with acute sudden-onset  
289 severe headache, HIV-positive patients presenting with a new or different headache, and pregnant patients. Acute  
290 sudden-onset, severe headache (sometimes referred to in the literature as thunderclap headache) prompts concerns  
291 for subarachnoid hemorrhage or other serious intracranial pathology. The term thunderclap headache, first used by  
292 Day and Raskin,<sup>33</sup> describes a sudden-onset headache whose intensity is severe (usually described as worst of life,  
293 or excruciating) and reaches that maximal intensity within seconds to a minute. There are many causes of  
294 thunderclap headache, many of them serious.<sup>34</sup> The term “sudden-onset severe headache” will be used  
295 synonymously with thunderclap headache in the remainder of this document.

296         Although most patients with sudden-onset severe headache have benign causes, the best data suggest that  
297 between 10% and 15% have more serious pathology, most commonly subarachnoid hemorrhage.<sup>35-38</sup> Mitchell et  
298 al<sup>28</sup> reported on 27 patients with the “worst headache of their life,” and only 1 had intracranial pathology.  
299 Ramirez-Lassepas et al<sup>30</sup> reviewed 468 headache patient records and found no association between the patient’s  
300 description of the headache and the final diagnosis. Reinus et al<sup>39</sup> retrospectively studied 333 patients with an  
301 acute headache; 17 presented with the “worst headache of their life” complaint, yet only 1 had positive findings

302  
303 when a head CT was performed (lumbar puncture results were not reported). Conversely, Harling et al<sup>25</sup>  
304 prospectively studied patients presenting with a thunderclap headache; of 49 patients, 35 had a subarachnoid  
305 hemorrhage. Lledo et al<sup>24</sup> prospectively studied all patients presenting during a 1-year period with severe sudden-  
306 onset headache. Of 27 patients enrolled, 9 had subarachnoid hemorrhage, 1 had intraventricular hemorrhage, and  
307 2 had meningitis. Only 4 of the 9 patients had positive CT results, but patients in this study were late presenters  
308 (mean delay 72 hours after onset of headache for the subarachnoid hemorrhage patients). In a prospective study,  
309 Mills et al<sup>29</sup> reported that 29% of patients complaining of the “worst headache of their life” had positive findings  
310 on head CT scan. When the headache is described as a thunderclap headache, it is still recommended that the  
311 patient undergo emergent neuroimaging followed by a cerebrospinal fluid (CSF) analysis. This topic is more  
312 thoroughly discussed in Question 3.

313         In the United States, the overall decreased incidence of HIV seroconversion combined with improved  
314 antiviral therapy has decreased the number of acutely ill HIV patients seen in the ED. Yet, as the disease  
315 advances, patients with HIV disease frequently have central nervous system processes that include space-  
316 occupying lesions. Lipton et al<sup>40</sup> reported on 49 HIV patients presenting with a chief complaint of headache, 35%  
317 of whom were found to have a mass lesion. Rothman et al<sup>41</sup> prospectively studied 110 HIV patients with  
318 neurologic complaints, searching for predictors of new focal central nervous system lesions. Twenty-four percent  
319 of the patients were found to have a focal lesion. Using multivariate logistic regression analysis, new seizure,  
320 depressed or altered orientation, and headache that was different in character from previous ones or that lasted  
321 more than 3 days predicted a focal brain lesion. The presence of 1 or more of these 4 clinical findings identified  
322 all patients with focal lesions; these data have not been prospectively validated. As reported in other headache  
323 studies, focal motor deficit had a strong univariate association, with a positive predictive value of 41.7 and a *P*  
324 value of .02.<sup>41</sup>

325         During pregnancy and the puerperium, it has been reported that the incidence of stroke increases 3- to 13-  
326 fold.<sup>42</sup> Headache is frequently the symptom that prompts an emergent evaluation in these patients. The majority of  
327 pregnant women with headaches have benign causes. In one non-ED series of more than 1,100 pregnant women  
328 with headache, a very small number had serious secondary causes.<sup>43</sup> Although no reliable data exist, subarachnoid  
329 hemorrhage is thought to be increased during pregnancy, delivery and the puerperium, occurring in roughly 20

330  
331 per 100,000 deliveries.<sup>44</sup> Case reports illustrate other serious causes of headache such as carotid dissections,<sup>14</sup>  
332 venous sinus thrombosis,<sup>45</sup> and ruptured arteriovenous malformation.<sup>46</sup> Although these data illustrate the increased  
333 risk of adverse serious events in pregnant patients with headache who may present to the ED, there are  
334 insufficient data to drive any firm recommendations in this group of patients.

335 **3. Does lumbar puncture need to be routinely performed on ED patients being worked up for**  
336 **nontraumatic subarachnoid hemorrhage whose noncontrast brain CT scans are interpreted as normal?**

337 **Patient Management Recommendations**

338 *Level A recommendations.* None specified.

339 *Level B recommendations.* In patients presenting to the ED with sudden-onset, severe headache and a  
340 negative noncontrast head CT scan result, lumbar puncture should be performed to rule out subarachnoid  
341 hemorrhage.

342 *Level C recommendations.* None specified.

343  
344 Key words/phrases for literature searches: subarachnoid hemorrhage, acute imaging, lumbar puncture,  
345 and variations and combinations of the key words/phrases.

346  
347 The presenting symptom for subarachnoid hemorrhage for most patients presenting to the ED is a sudden,  
348 severe-onset headache unlike any previous episode.<sup>47</sup> The most common etiology of nontraumatic subarachnoid  
349 hemorrhage is the rupture of an aneurysm in the Circle of Willis. Because early, accurate detection of  
350 subarachnoid hemorrhage has been shown to improve outcomes, it is imperative that the clinician attempt to  
351 accurately identify these patients to prevent further morbidity and mortality.<sup>48,49</sup>

352 After a focused medical history and physical examination for the patient with a sudden-onset, severe  
353 headache, most patients undergo noncontrast CT imaging to rule out a subarachnoid hemorrhage. Noncontrast CT  
354 scanning in patients presenting to the ED for an acute headache has become increasingly easier to access. After a  
355 normal head CT scan result, patients with initially low pretest probability for subarachnoid hemorrhage may  
356 undergo additional testing, such as the lumbar puncture and CSF analysis. The lumbar puncture is considered the  
357 criterion standard for diagnosing subarachnoid hemorrhage because it may detect small amounts of  
358 xanthochromia or blood in the CSF that can be missed by CT.<sup>49-51</sup>

359 Xanthochromia, which is the yellow color caused by bilirubin and oxyhemoglobin due to lysis of  
360 erythrocytes, can be detected by either visual inspection or spectrophotometry. Because bilirubin formation is an  
361 enzyme-dependent, *in vivo* process, xanthochromia takes hours after the bleed to occur. Spectrophotometry is  
362 more sensitive, but this greater sensitivity comes at the expense of low-to-moderate specificity.<sup>52</sup> Furthermore,

363  
364 data suggests that clinicians using visual inspection identify those samples that contained significant amounts of  
365 bilirubin.<sup>53</sup> Finally, spectrophotometry is not available in the majority of North American hospital clinical  
366 laboratories.<sup>54</sup> Visual inspection of CSF for xanthochromia still requires proper technique. The CSF must be  
367 rapidly centrifuged, and the supernatant should be carefully compared to an identical tube filled with an equal  
368 volume of tap water against a white background.<sup>55</sup>

369         However, the lumbar puncture is an invasive procedure associated with patient discomfort because of  
370 needle insertion, local tissue irritation, and reflex muscle spasm, as well as complications such as postdural  
371 puncture headache, nerve injury, epidural hematoma, and meningitis. Furthermore, false-positive results lead to  
372 more invasive testing.<sup>56</sup> Morgenstern et al<sup>38</sup> found that emergency physicians omitted doing a lumbar puncture in  
373 patients for the work-up of their “worst headache of life” in 50% of cases.

374         Clinicians must understand the limitations of brain CT scanning. Limitations include (1) the technical  
375 inability of scanners to identify small hemorrhages in areas obscured by artifact or bone; (2) the inability to  
376 diagnose idiopathic intracranial hypertension, meningitis, or carotid or vertebral artery dissection, some cases of  
377 cerebral venous sinus thrombosis and pituitary apoplexy, and spontaneous intracranial hypotension; (3) the varied  
378 levels of expertise of the reader; (4) spectrum bias in small-volume subarachnoid hemorrhage; (5) decreased  
379 sensitivity for blood in the setting of anemia; and (6) decay in sensitivity with time.

380         As for spectrum bias, the sensitivity of CT is decreased for detecting subarachnoid hemorrhage in patients  
381 with “minor leaks” and those with normal neurologic examination results.<sup>57-59</sup> The sensitivity also decreases with  
382 time from onset of headache. This is because of the dilution and degradation of blood that occurs as CSF flows  
383 through the subarachnoid space. The International Cooperative Study on the Timing of Aneurysm Surgery  
384 evaluated 3,500 patients with aneurysmal subarachnoid hemorrhage with early 1980 CT scanners and found a  
385 decrease in positive scan results from 92% on the day of rupture to 86% at 1 day later, 76% at 2 days, and 58% 5  
386 days later.<sup>59</sup> Several additional studies using modern CT scanners have shown a consistent decrease in sensitivity  
387 in detecting blood as time elapses from symptom onset.<sup>38,60,61</sup> Last, as the hematocrit level decreases, blood will  
388 appear isodense with brain tissue and can be easily overlooked by the reviewer; this occurs at hemoglobin  
389 concentrations below 10 g/dL.<sup>62</sup>

390

391

392           Recent advances in CT technology have improved the accuracy of CT scans compared with third-  
393 generation scanners from the 1980s and 1990s. Previous sensitivities in these scanners for detecting subarachnoid  
394 hemorrhage have been from 92% to 98%.<sup>38,60,61</sup>

395           The lumbar puncture also has well-defined limitations in diagnosing subarachnoid hemorrhage and other  
396 significant intracranial pathologic entities. These include unruptured aneurysm, arterial dissection or cerebral  
397 venous sinus thrombosis, and pituitary apoplexy, all of which can present in a manner similar to subarachnoid  
398 hemorrhage and which may not be identified if only a lumbar puncture is performed. The lumbar puncture may be  
399 time consuming and can be technically difficult in uncooperative or obese patients. Contamination of the CSF  
400 with venous blood introduced during the procedure may make interpretation of CSF difficult. The Class III study  
401 by Shah et al<sup>63</sup> found the incidence of traumatic lumbar puncture in the ED was 13.3%, using 400 RBCs as the  
402 cutoff and 8.9% using 1,000 RBCs as the cutoff with higher percentages when the lumbar puncture was done on  
403 the inpatient service. Finally, there is morbidity, including the risk of postdural puncture headache.<sup>64</sup> Additional  
404 potential information from the lumbar puncture that often goes unused is an initial opening pressure. Measuring  
405 the opening pressure can be helpful in distinguishing a traumatic puncture from a true subarachnoid hemorrhage  
406 (in which two thirds of cases show an elevated pressure), as well as for providing additional information for other  
407 diagnoses such as spontaneous intracranial hypotension, benign intracranial hypertension, and cerebral venous  
408 sinus thrombosis, all of which can present with severe headache.<sup>50,65-67</sup>

409           Several studies have attempted to quantify the value of CT scanning and lumbar puncture in patients with  
410 suspected subarachnoid hemorrhage. Previous estimates have found rates of subarachnoid hemorrhage confirmed  
411 by lumbar puncture (after normal CT scan results) of 2.5% to 3.5%.<sup>58</sup> In a Class II study of 592 patients  
412 presenting to the ED with acute, severe headache, 61 had subarachnoid hemorrhage; of these, 55 were diagnosed  
413 by CT and 6 by lumbar puncture.<sup>68</sup> Foot and Staib<sup>69</sup> performed a retrospective chart review (Class III) of 196  
414 patients who had CSF analysis to risk stratify for subarachnoid hemorrhage with a normal or equivocal CT scan  
415 result. Only 1 of 189 patients with a negative CT scan result had subarachnoid hemorrhage (0.5; 95% CI 0% to  
416 2.9%). Three other patients had “benign subarachnoid hemorrhage” (likely angiogram-negative,  
417 perimesencephalic subarachnoid hemorrhage). In another Class III study, O’Neill et al<sup>70</sup> retrospectively reviewed  
418 127 patients presenting to the ED with acute headache, 19 of whom had subarachnoid hemorrhage, of whom 6

419  
420 were diagnosed by lumbar puncture showing xanthochromia. All 6 patients underwent angiography; 4 results  
421 were normal and 2 showed aneurysms.

422         Advanced imaging techniques are increasingly available that may facilitate more accurate and timely  
423 diagnosis of disease in the acute headache patient. Boesinger and Shiber<sup>71</sup> performed a Class III retrospective  
424 chart review of ED headache patients during a 1-year period who had both a CT scan (fifth generation, multislice  
425 detector) and lumbar puncture. Of the 177 patients who were analyzed, no patient with a negative CT scan result  
426 had a subarachnoid hemorrhage. However, a more recent Class III study of 149 patients with subarachnoid  
427 hemorrhage, which also used a multislice scanner, found a sensitivity for CT of 93% for all patients and a  
428 sensitivity of 90% for those less affected patients presenting with headache and a normal mental status.<sup>72</sup> The  
429 totality of the evidence suggests that lumbar puncture must still be performed after a negative CT scan result in  
430 patients being evaluated for subarachnoid hemorrhage.

431         Despite the relatively rapid advancement of imaging technology available to the emergency physician, the  
432 diagnosis of severe headache is challenging and often requires a high degree of suspicion and clinical acumen. To  
433 date, no single noninvasive imaging modality is 100% sensitive in detecting acute subarachnoid hemorrhage and  
434 the other significant intracranial lesions responsible for the severe headache presentation. In the future, additional  
435 studies will need to focus on the decisionmaking process, accurate risk stratification, pre- and posttest disease  
436 probability and Bayesian analysis, allowing for the proper use of technology to aid in the decision process to rule  
437 out subarachnoid hemorrhage in the severe headache patient.

438 **4. In which adult patients with a complaint of headache can a lumbar puncture be safely performed**  
439 **without a neuroimaging study?**

440 **Patient Management Recommendations**

441         *Level A recommendations.* None specified.

442         *Level B recommendations.* None specified.

443         *Level C recommendations.*

444         1. Adult patients with headache and exhibiting signs of increased intracranial pressure (eg, papilledema,  
445 absent venous pulsations on funduscopic examination, altered mental status, focal neurologic deficits, signs of  
446 meningeal irritation) should undergo a neuroimaging study before having a lumbar puncture.

447         2. In the absence of clinical findings suggestive of increased intracranial pressure, a lumbar puncture can  
448 be performed without obtaining a neuroimaging study. (*Note: A lumbar puncture does not assess for all causes of*  
449 *a sudden severe headache.*)

450  
451         Key words/phrases for literature searches: acute headache, lumbar puncture, subarachnoid hemorrhage,  
452 neuroimaging, head CT, diagnostic imaging, and variations and combinations of the key words/phrases.

453  
454           In patients with acute headache, head CT and CSF analysis are used alone and in combination to diagnose  
455 life-threatening entities, including mass lesions, intracranial hemorrhage, and infection. There are times when  
456 CSF analysis alone would suffice; however, concern of causing herniation because of increased intracranial  
457 pressure often prompts obtaining a head CT scan before a lumbar puncture. To choose the appropriate diagnostic  
458 study, it is important to know the indications and limitations of the study. If a CSF analysis is the only test  
459 needed, it is important to recognize which patients can have a lumbar puncture safely performed without risk of  
460 herniation.

461           The risk of herniation has been the paramount concern of clinicians who perform lumbar punctures. The  
462 earliest description of this complication was reported 6 years after Heinrich Quincke performed the first lumbar  
463 puncture in 1890.<sup>64</sup> Four deaths resulting from herniation were reported by Furbinger in 1896; the increased  
464 intracranial pressure was attributed to cerebellar neoplasms in 2 cases, to a cerebellar abscess in 1 case, and to a  
465 frontal tumor in 1 case.<sup>64</sup> Although herniation is a rare occurrence overall, other case reports have been published  
466 since these earliest observations describing cerebral herniation resulting from the performance of a lumbar  
467 puncture.<sup>73</sup> Interestingly, one study of a small number of patients with intracranial pressure monitors in place  
468 suggested that intracranial pressure could be estimated by measurement of intraocular pressure.<sup>74</sup>

469           There are no prospective, controlled trials testing the safety of performing a lumbar puncture before a  
470 neuroimaging study in patients with a chief complaint of headache. One study addressed this question using a  
471 mathematical model in which lumbar puncture would be the first diagnostic test for the acute-onset headache  
472 patient with suspected subarachnoid hemorrhage and found that for every 100 patients, the “lumbar puncture  
473 first” model would result in significantly fewer CT scans (79 to 83) and a few additional lumbar punctures (7 to  
474 11).<sup>75</sup> This hypothesis has never been tested in a clinical trial. For ethical reasons, it is unlikely that patients with  
475 focal neurologic findings, altered mental status, or other evidence of increased intracranial pressure will ever be  
476 enrolled as subjects in a controlled trial in which a lumbar puncture is performed before a neuroimaging study.

477           Two case series by Duffy<sup>76,77</sup> describe occurrences of herniation in patients with known or strongly  
478 suspected intracranial hematomas. In one report, 10 of 30 patients stopped breathing or developed unequal pupils  
479 while the lumbar puncture needle was still in place or shortly after it was removed.<sup>76</sup> Fifteen of the 30 patients had  
480 marked deterioration within 24 hours of the procedure. The relative contributions of the lumbar puncture versus

481  
482 the natural disease course to the patients' clinical deterioration is not known. All 30 patients in this report had  
483 significant clinical findings such as a focal neurologic examination, progressive mental status changes,  
484 papilledema, "meningitic symptoms," or abnormal cranial radiographs. In another case series, 44 of 74 patients  
485 underwent lumbar puncture before neuroimaging.<sup>77</sup> All of the patients were drowsy, confused, or had neurologic  
486 deficits. Seven had clinical deterioration at the time of lumbar puncture, and all of these had an intracranial  
487 hematoma.

488 A case series reported from Australia in 1985 described lumbar puncture in 70 patients who had a "mild  
489 hemiparesis," had drowsiness, or were confused.<sup>78</sup> Only 1 of the 70 patients, a patient with a subarachnoid  
490 hemorrhage, deteriorated after the lumbar puncture and died 12 days later.

491 Whereas Duffy's case series<sup>76,77</sup> suggest the high likelihood of an adverse outcome if a patient with a  
492 space-occupying lesion undergoes a lumbar puncture, a 1988 Class III report by Zisfein and Tuchman<sup>79</sup> had the  
493 opposite finding. Thirty-eight patients with head CTs demonstrating an intracranial mass underwent lumbar  
494 puncture "to rule out meningitis." All patients had an abnormal mental status or focal neurologic examination  
495 before undergoing the procedure. Thirty-four patients (89%) had evidence of a mass effect on head CT. The  
496 central nervous system pathologic processes included hematomas, abscesses, and dural collections. No significant  
497 neurologic deterioration was noted in 37 of 38 patients. One patient who had no brainstem function (absent  
498 caloric reflexes, dilated and fixed pupils) before the lumbar puncture died after the procedure.

499 Patients with a headache, a normal neurologic examination, a normal mental status, a normal funduscopic  
500 examination, and no meningeal signs are theoretically the best candidates for the "lumbar puncture without CT"  
501 strategy. To characterize patients who could safely undergo a lumbar puncture without prior neuroimaging,  
502 researchers at Duke University Medical Center, in a Class II study, asked internal medicine residents supervised  
503 by ED attendings, to complete standard forms before CT scan of all patients who presented to the ED and needed  
504 an emergent lumbar puncture.<sup>80</sup> The reasons for emergent lumbar puncture were suspected meningitis (37%),  
505 suspected subarachnoid hemorrhage (42%), and other (21%). The physicians recorded their impression of the  
506 likelihood that a patient would have a CT finding that contraindicated dural puncture. Seventeen of 111 enrolled  
507 patients had a new central nervous system abnormality. Three of these 17 had contraindications to spinal tap (as  
508 defined by CT findings). Clinical findings that predicted abnormal CT results with statistical significance were

509  
510 altered mental status (positive LR [+LR] 2.2; 95% CI 1.5 to 3.2), papilledema (+LR 11.1; 95% CI 1.1 to 115), and  
511 focal neurologic findings (+LR 4.3; 95% CI 1.9 to 10). The physician's clinical impression had the highest  
512 predictive value in identifying patients with a contraindication to lumbar puncture (+LR 18.8; 95% CI 4.8 to 43).  
513 Clinicians identified the 3 patients with contraindications to lumbar puncture. Clinical attributes, including the  
514 diagnosis of HIV disease or having HIV risk factors, history of a central nervous system mass lesion, or a history  
515 of malignant neoplasm, were not statistically significant in predicting patients in whom a lumbar puncture was  
516 contraindicated, a finding that could be a consequence of the study's small sample size. The study did not  
517 specifically address patients suspected of having subarachnoid hemorrhage, nor did it provide outcome data using  
518 a "lumbar puncture first" strategy; therefore, a uniformly favorable result cannot be assumed without prospective  
519 validation studies.

520 **5. Is there a need for further emergent diagnostic imaging in the patient with sudden-onset, severe**  
521 **headache who has negative findings in both CT and lumbar puncture?**

522 **Patient Management Recommendations**

523 *Level A recommendations.* None specified.

524 *Level B recommendations.* Patients with a sudden-onset, severe headache who have negative findings on  
525 a head CT, normal opening pressure, and negative findings in CSF analysis do not need emergent angiography  
526 and can be discharged from the ED with follow-up recommended.

527 *Level C recommendations.* None specified.

528  
529  
530 Key words/phrases for literature searches: headache, thunderclap headache, emergency angiography,  
531 cerebrovascular disorders, glaucoma (acute angle closure), meningitis, brain neoplasm, temporal arteritis,  
532 pseudotumore cerebri, hypertensive encephalopathy, carbon monoxide poisoning, medical errors, and variations  
533 and combinations of the key words/phrases.

534 Because patients with sudden-onset, severe headache due to subarachnoid hemorrhage and those due to  
535 benign causes cannot be distinguished clinically,<sup>47</sup> all patients with sudden-onset, severe headache require a work-  
536 up for subarachnoid hemorrhage (noncontrast CT scan and a lumbar puncture looking for blood or xanthochromia  
537 if the CT result is normal or nondiagnostic). It is important to emphasize that there is a differential diagnosis to  
538 sudden-onset, severe headache beyond simply subarachnoid hemorrhage and benign causes and therefore, in  
539 patients whose presentations suggest other causes such as pituitary apoplexy, cerebral venous sinus thrombosis,  
540 arterial dissections, and cerebellar stroke, further diagnostic testing may be indicated.<sup>34,81</sup>

541 The current teaching is that if both tests yield negative results, subarachnoid hemorrhage is ruled out.<sup>82</sup>  
542 The timing of the lumbar puncture may be critical in this decisionmaking process. It has been suggested that  
543 lumbar punctures performed prior to 12 hours from onset of symptoms may give false-negative results either

544 because blood has not diffused down or because sufficient time has not elapsed to allow for xanthochromia to  
545 appear.<sup>50</sup> Older data collected from the pre-CT era, when lumbar puncture was the primary method to diagnose  
546 subarachnoid hemorrhage, show that even in those patients undergoing lumbar puncture in the first 12 hours after  
547 headache onset, all had RBCs in the lumbar theca. Also, 60% (43 of 72 patients for whom a result was recorded)  
548 had xanthochromia (by visual inspection) even when measured within 12 hours.<sup>83</sup>

549         The notion of performing cerebral angiography in patients with thunderclap headache, even after negative  
550 CT results and CSF analysis, has historically been controversial and remains unsettled. It is theorized that either  
551 hemorrhage into the wall of the aneurysm or rapid aneurysmal expansion or thrombosis can cause an acute  
552 headache. Therefore, some investigators still believe that normal findings in both a CT scan and lumbar puncture  
553 are not enough to exclude an aneurysmal cause of thunderclap headache. The widespread availability of  
554 multimodal CT and MRI has led to many centers using these techniques in the next step in the evaluation of the  
555 sudden-onset, severe headache patient with an initially normal evaluation. Because neither CT nor MRI can  
556 exclude subarachnoid hemorrhage with 100% reliability, CT and lumbar puncture is still considered the standard  
557 method to evaluate these patients. Although it is clear that noninvasive imaging, including angiography, will  
558 sometimes diagnose the other medical conditions mentioned above, they will also diagnose incidental aneurysms  
559 in 2% to 6% of the general population that are not causing the patient's symptoms and which will result in more  
560 unnecessary diagnostic and therapeutic procedures.

561         A primary concern of most clinicians is the short-term outcome of the acute headache patient presenting  
562 to the ED. The most effective evaluation is one that identifies all acute illness and any underlying lesions that  
563 place these patients at further risk for an adverse outcome. In the setting of sudden-onset, severe headache, no  
564 subarachnoid hemorrhage or sudden death during a 1-year follow-up has been used as a proxy outcome measure.

565         The largest study addressing this issue is by Perry et al,<sup>68</sup> who published a Class II study of 592 patients  
566 with acute severe headache presenting to 2 Canadian EDs and who had a CT and lumbar puncture; 61 (10.3%)  
567 had subarachnoid hemorrhage. They followed the patients with negative CT and lumbar puncture results for 6 to  
568 36 months; none was found to have a subsequent subarachnoid hemorrhage, although a single patient was later  
569 found to have an unruptured aneurysm that the treating neurosurgeon did not think was related to the earlier  
570 headache.

571         Two other, smaller Class II studies have shown similar results in patients followed up at 1 year. In 2002,  
572 Landtblom et al<sup>37</sup> published a Class II prospective cohort study on 137 consecutive patients with sudden-onset,

573 severe headache and presenting to the ED in Sweden. The study was accomplished in 2 phases. During the second  
574 phase of their study, which was designed to measure the frequency of subarachnoid hemorrhage, 9 of 80 (11%)  
575 patients had subarachnoid hemorrhage. Patients whose work-up for subarachnoid hemorrhage (CT and lumbar  
576 puncture) was negative were followed for 1 year; none went on to have a subsequent subarachnoid hemorrhage.  
577 They concluded that angiography is not routinely necessary in this group of patients.

578 In 1994, a Class II study by Linn et al<sup>35</sup> reported on 148 patients with acute severe headache. Of this  
579 group, 103 patients had acute severe headache and no other neurologic findings. Of the 103, 12 (12%) had  
580 subarachnoid hemorrhage and 4 had other neurologic diagnoses established in their workups. Of the patients for  
581 whom no diagnosis was made by CT and lumbar puncture, none was found to have subarachnoid hemorrhage or  
582 sudden death during 1 year of follow-up.

583 Wijdicks et al<sup>36</sup> conducted a Class III retrospective follow-up study during a 3.3-year period on 71  
584 patients, each of whom presented with a thunderclap headache with negative findings for subarachnoid  
585 hemorrhage in both a CT scan and lumbar puncture. Angiograms were performed on 6 of 71 patients; all results  
586 were negative. None of 71 patients had subarachnoid hemorrhage during the 3.3-year follow-up period.

587 Furthermore, Harling et al<sup>25</sup> performed a small, Class III, prospective study on 49 patients with  
588 thunderclap headache. Fourteen of 49 patients presenting with thunderclap headaches had negative findings on  
589 both a CT scan and lumbar puncture. These patients were followed for a minimum of 18 months, and none had  
590 subarachnoid hemorrhage.

591 The previous studies must be balanced by several case reports and case series that indicate that some  
592 patients with unruptured aneurysms (but not subarachnoid hemorrhage) can present with acute severe  
593 headache.<sup>33,84-87</sup> In the first of these reports,<sup>33</sup> an angiogram showed cerebral vasospasm and an unruptured  
594 aneurysm. Because patients with “benign thunderclap headache” have been shown to have vasospasm in the  
595 absence of aneurysms,<sup>88,89</sup> the aneurysm in this case may have been an incidental finding. Taken together, these 5  
596 studies suggest that in some patients with severe, sudden-onset headaches in the setting of a normal brain CT and  
597 CSF evaluation, aneurysmal expansion, thrombosis, or intramural hemorrhage can be the cause of their  
598 headaches. When these patients are evaluated, it is important to factor in the time from symptom onset to the time  
599 of the diagnostic tests because early or late testing will affect the results.<sup>50</sup>

600 With the increased availability of advanced CT multimodal imaging in the ED, emergency physicians  
601 have an enhanced ability to obtain information in properly selected patients. Carstairs et al<sup>90</sup> conducted a Class II

602 study assessing the ability of CT angiography, along with CT and lumbar puncture, to diagnose subarachnoid  
603 hemorrhage in ED patients presenting with headache. This study used CT angiography, in addition to standard CT  
604 and lumbar puncture, to assist in the diagnosis of subarachnoid hemorrhage. Of 106 patients completing the study  
605 (of the 116 enrolled), 6 were found to have aneurysms by CT angiography, which is close to the prevalence that  
606 would be expected from autopsy figures.<sup>91</sup> Of those 6, 3 had either a positive CT or lumbar puncture result. Of the  
607 remaining 3, 1 was found to have a false-positive CT angiography result and 1 patient declined surgery and  
608 remained asymptomatic, suggesting she had an incidental aneurysm. This study has several limitations, the most  
609 important of which is the unproven assumption that the simultaneous presence of an aneurysm and a headache  
610 equates with subarachnoid hemorrhage. The strategy of using advanced imaging techniques in the ED evaluation  
611 of headache is unproven but merits additional study.

612

613 ***Relevant industry relationships of subcommittee members: There were no relevant industry***  
614 ***relationships disclosed by the subcommittee members.***

615 ***Relevant industry relationships are those relationships with companies associated with products or***  
616 ***services that significantly impact the specific aspect of disease addressed in the critical question.***

## 617 REFERENCES

618

- 619 1. Goldstein JN, Camargo CA Jr, Pelletier AJ, et al. Headache in United States emergency departments:  
620 demographics, work-up and frequency of pathological diagnoses. *Cephalalgia*. 2006;26:684-690.  
621
- 622 2. American College of Emergency Physicians. Clinical policy: critical issues in the evaluation and  
623 management of patient presenting to the emergency department with acute headache. *Ann Emerg Med*.  
624 2002;39:108-122.  
625
- 626 3. Perry JJ, Stiell IG, Wells GA, et al. Attitudes and judgment of emergency physicians in the management  
627 of patients with acute headache. *Acad Emerg Med*. 2005;12:33-37.  
628
- 629 4. Schriger DL, Cantrill SV, Greene CS. The origins, benefits, harms, and implications of emergency  
630 medicine clinical policies. *Ann Emerg Med*. 1993;22:597-602.  
631
- 632 5. Diamond S. Head pain: diagnosis and management. *Clin Symp*. 1994;46:1-34.  
633
- 634 6. Moskowitz MA. Neurogenic inflammation in the pathophysiology and treatment of migraine.  
635 *Neurology*. 1993;43(suppl 3):S16-S20.  
636
- 637 7. Lance JW. Current concepts of migraine pathogenesis. *Neurology*. 1993;43(suppl 3):S11-S15.  
638
- 639 8. Peroutka SJ. 5-Hydroxytryptamine receptor subtypes and the pharmacology of migraine. *Neurology*.  
640 1993;43(suppl 3):S34-S38.  
641
- 642 9. US Headache Consortium. Evidence-based treatment guidelines for migraine headache in the primary  
643 care setting: pharmacological management of acute attacks. American Academy of Neurology, 2000.  
644 Available at: <http://www.aan.com>. Accessed January 1, 2001.  
645
- 646 10. Seymour JJ, Moscatti RM, Jehle DV. Response of headaches to nonnarcotic analgesics resulting in missed

- 647 intracranial hemorrhage. *Am J Emerg Med.* 1995;13:43-45.  
648
- 649 11. Gross DW, Donat JR, Boyle CA. Dihydroergotamine and metoclopramide in the treatment of organic  
650 headache. *Headache.* 1995;35:637-638.  
651
- 652 12. Lipton RB, Mazer C, Newman LC, et al. Sumatriptan relieves migraine-like headaches associated with  
653 carbon monoxide exposure. *Headache.* 1997;37:392-395.  
654
- 655 13. Agostoni E. Headache in cerebral venous thrombosis. *Neurol Sci.* 2004;25:S206-S210.  
656
- 657 14. Abisaab J, Nevadunsky N, Flomenbaum N. Emergency department presentation of bilateral carotid artery  
658 dissections in a postpartum patient. *Ann Emerg Med.* 2004;44:484-489.  
659
- 660 15. Leira EC, Cruz-Flores S, Leacock RO, et al. Sumatriptan can alleviate headaches due to carotid artery  
661 dissection. *Headache.* 2001;41:590-591.  
662
- 663 16. Pfadenhauer K, Schonsteiner T, Keller H. The risks of sumatriptan administration in patients with  
664 unrecognized subarachnoid haemorrhage (SAH). *Cephalalgia.* 2006;26:320-323.  
665
- 666 17. Rothrock J. The perils of misinterpreting a treatment response. *Headache.* 2005;45:599-600.  
667
- 668 18. Wang K-C, Fuh J-L, Lirng J-F, et al. Headache profiles in patients with a dilated cyst of the cavum septi  
669 pellucidi. *Cephalalgia.* 2004;24:867-874.  
670
- 671 19. American College of Emergency Physicians, American Academy of Neurology, American Association of  
672 Neurological Surgeons, American Society of Neuroradiology. Practice parameter: neuroimaging in the  
673 patient presenting with seizure. *Ann Emerg Med.* 1996;28:114-118.  
674
- 675 20. Fitzpatrick R, Hopkins A. Referrals to neurologists for headaches not due to structural disease. *J Neurol*  
676 *Neurosurg Psychiatry.* 1981;44:1061-1067.  
677
- 678 21. American Academy of Neurology. Practice parameter: the utility of neuroimaging in the evaluation of  
679 headache in patients with normal neurologic examinations. *Neurology.* 1994;44:1353-1354.  
680
- 681 22. US Headache Consortium. Evidence-based guidelines in the primary care setting: neuroimaging in  
682 patients with nonacute headache. American Academy of Neurology, 2000. Available at:  
683 <http://www.aan.com>. Accessed January 1, 2001.  
684
- 685 23. American College of Emergency Physicians. Clinical policy for the initial approach to adolescents and  
686 adults presenting to the emergency department with a chief complaint of headache. *Ann Emerg Med.*  
687 1996;27:821-844.  
688
- 689 24. Lledo A, Calandre L, Marinez-Menendez B, et al. Acute headache of recent onset and subarachnoid  
690 hemorrhage: a prospective study. *Headache.* 1994;34:172-174.  
691
- 692 25. Harling DW, Peatfield RC, Van Hille PT, et al. Thunderclap headache: is it migraine? *Cephalalgia.*  
693 1989;9:87-90.  
694
- 695 26. Akpek S, Arac M, Atilla S, et al. Cost-effectiveness of computed tomography in the evaluation of patients  
696 with headache. *Headache.* 1995;35:228-230.  
697
- 698 27. Demaerel P, Boelaert I, Wilms G, et al. The role of cranial computed tomography in the diagnostic work-  
699 up of headache. *Headache.* 1996;36:347-348.  
700  
701

- 702  
703 28. Mitchell CS, Osborn RE, Grosskreutz SR. Computed tomography in the headache patient: is routine  
704 evaluation really necessary? *Headache*. 1993;33:82-86.  
705
- 706 29. Mills ML, Russo LS, Vines FS, et al. High yield criteria for urgent cranial computed tomography scans.  
707 *Ann Emerg Med*. 1986;15:1167-1172.  
708
- 709 30. Ramirez-Lassepas M, Espinosa CE, Cicero JJ, et al. Predictors of intracranial pathologic findings in  
710 patients who seek emergency care because of headache. *Arch Neurol*. 1997;54:1506-1509.  
711
- 712 31. Kahn CE, Sanders GD, Lyons EA, et al. Computed tomography for nontraumatic headache: current  
713 utilization and cost-effectiveness. *Can Assoc Radiol J*. 1993;44:189-193.  
714
- 715 32. Duarte J, Sempere AP, Delgado JA, et al. Headache of recent onset in adults: a prospective population-  
716 based study. *Acta Neurol Scand*. 1996;94:67-70.  
717
- 718 33. Day JW, Raskin NH. Thunderclap headache: symptom of unruptured cerebral aneurysm. *Lancet*.  
719 1986;2:1247-1248.  
720
- 721 34. Schwedt TJ, Matharu MS, Dodick DW. Thunderclap headache. *Lancet Neurol*; 2006;5:621-631.  
722
- 723 35. Linn FHH, Wijdicks EFM, van der Graaf Y, et al. Prospective study of sentinel headache in aneurysmal  
724 subarachnoid haemorrhage. *Lancet*. 1994;344:590-593.  
725
- 726 36. Wijdicks EF, Kerkhoff H, van Gijn J. Long-term follow-up of 71 patients with thunderclap headache  
727 mimicking subarachnoid haemorrhage. *Lancet*. 1988;2:68-70.  
728
- 729 37. Landtblom A-M, Fridriksson S, Boivie J, et al. Sudden onset headache: a prospective study of features,  
730 incidence and causes. *Cephalalgia*. 2002;22:354-360.  
731
- 732 38. Morgenstern LB, Luna-Gonzales H, Huber JC Jr, et al. Worst headache and subarachnoid hemorrhage:  
733 prospective, modern computed tomography and spinal fluid analysis. *Ann Emerg Med*. 1998;32:297-304.  
734
- 735 39. Reinus WR, Wippold FJ, Erickson KK. Practical selection criteria for unenhanced cranial CT in patients  
736 with acute headache. *Emerg Radiol*. 1994;1:81-84.  
737
- 738 40. Lipton RB, Feraru ER, Weiss G, et al. Headache in HIV-1 related disorders. *Headache*. 1991;31:518-522.  
739
- 740 41. Rothman RE, Keyl PM, McArthur JC, et al. A decision guideline for emergency department utilization of  
741 noncontrast head computed tomography in HIV-infected patients. *Acad Emerg Med*. 1999;6:1010-1019.  
742
- 743 42. Sharshar T, Lamy C, Mas JL, for the Stroke in Pregnancy Study Group. Incidence and causes of strokes  
744 associated with pregnancy and puerperium. A study in public hospitals of Ile de France. *Stroke*.  
745 1995;26:930-936.  
746
- 747 43. Melhado EM, Maciel JA Jr, Guerreiro CA. Headache during gestation: evaluation of 1,101 women. *Can J*  
748 *Neurol Sci*. 2007;34:187-192.  
749
- 750 44. Selo-Ojeme DO, Marshman LA, Ikomi A, et al. Aneurysmal subarachnoid haemorrhage in pregnancy.  
751 *Eur J Obstet Gynecol Reprod Biol*. 2004;116:131-143.  
752
- 753 45. DeLashaw MR, Vizioli TL Jr, Counselman FL. Headache and seizure in a young woman postpartum. *J*  
754 *Emerg Med*. 2005;29:289-293.  
755  
756

- 757  
758 46. English LA, Mulvey DC. Ruptured arteriovenous malformation and subarachnoid hemorrhage during  
759 emergent cesarean delivery: a case report. *AANA J*. 2004;72:423-426.  
760
- 761 47. Linn FH, Rinkel GJ, Algra A, et al. Headache characteristics in subarachnoid haemorrhage and benign  
762 thunderclap headache. *J Neurol Neurosurg Psychiatry*. 1998;65:791-793.  
763
- 764 48. Edlow JA. Diagnosis of subarachnoid hemorrhage in the emergency department. *Emerg Med Clin North*  
765 *Am*. 2003;21:73-87.  
766
- 767 49. Edlow JA. Diagnosis of subarachnoid hemorrhage. *Neurocrit Care*. 2005;2:99-109.  
768
- 769 50. Edlow JA, Caplan LR. Avoiding pitfalls in the diagnosis of subarachnoid hemorrhage. *N Engl J Med*.  
770 2000;342:29-36.  
771
- 772 51. van Gijn J, Kerr RS, Rinkel GJ. Subarachnoid haemorrhage. *Lancet*. 2007;369:306-318.  
773
- 774 52. Perry JJ, Sivilotti MLA, Stiell IG, et al. Should spectrophotometry be used to identify xanthochromia in  
775 the cerebrospinal fluid of alert patients suspected of having subarachnoid hemorrhage? *Stroke*.  
776 2006;37:2467-2472.  
777
- 778 53. Linn FH, Voorbij HA, Rinkel GJ, et al. Visual inspection versus spectrophotometry in detecting bilirubin  
779 in cerebrospinal fluid. *J Neurol Neurosurg Psychiatry*. 2005;76:1452-1454.  
780
- 781 54. Edlow JA, Bruner KS, Horowitz GL. Xanthochromia. *Arch Pathol Lab Med*. 2002;126:413-415.  
782
- 783 55. Edlow JA, Malek AM, Ogilvy CS. Aneurysmal subarachnoid hemorrhage: update for emergency  
784 physicians. *J Emerg Med*. 2008;34:237-251.  
785
- 786 56. Kuntz KM, Kokmen E, Stevens JC, et al. Post-lumbar puncture headaches: experience in 501 consecutive  
787 procedures. *Neurology*. 1992;42:1884-1887.  
788
- 789 57. Leblanc R. The minor leak preceding subarachnoid hemorrhage. *J Neurosurg*. 1987;66:35-39.  
790
- 791 58. van der Wee N, Rinkel GJ, Hasan D, et al. Detection of subarachnoid haemorrhage on early CT: is lumbar  
792 puncture still needed after a negative scan? *J Neurol Neurosurg Psychiatry*. 1995;58:357-359.  
793
- 794 59. Kassell NF, Tomer JC, Haley EC Jr, et al. The International Cooperative Study on the Timing of  
795 Aneurysm Surgery. Part 1: overall management results. *J Neurosurg*. 1990;73:18-36.  
796
- 797 60. Sidman R, Connolly E, Lemke T. Subarachnoid hemorrhage diagnosis: lumbar puncture is still needed  
798 when the computed tomography scan is normal. *Acad Emerg Med*. 1996;3:827-831.  
799
- 800 61. Sames TA, Storrow AB, Finkelstein JA, et al. Sensitivity of new-generation computed tomography in  
801 subarachnoid hemorrhage. *Acad Emerg Med*. 1996;3:16-20.  
802
- 803 62. Smith WP, Batnitzky S, Rengachary SS. Acute isodense subdural hematomas: a problem in anemic  
804 patients. *AJR Am J Roentgenol*. 1981;136:543-546.  
805
- 806 63. Shah KH, Richard KM, Nicholas S, et al. Incidence of traumatic lumbar puncture. *Acad Emerg Med*.  
807 2003;10:151-154.  
808
- 809 64. Evans RW. Complications of lumbar puncture. *Neurol Clin*. 1998;16:83-105.  
810
- 811 65. Schievink WI. Misdiagnosis of spontaneous intracranial hypotension. *Arch Neurol*. 2003;60:1713-1718.

- 812  
813 66. Fridriksson S, Hillman J, Landtblom A-M, et al. Education of referring doctors about sudden onset  
814 headache in subarachnoid hemorrhage. *Acta Neurol Scand.* 2001;103:238-242.  
815
- 816 67. Quattrone A, Bono F, Oliveri RL, et al. Cerebral venous thrombosis and isolated intracranial  
817 hypertension without papilledema in CDH. *Neurology.* 2001;57:31-36.  
818
- 819 68. Perry JJ, Spacek A, Forbes M, et al. Is the combination of negative computed tomography result and  
820 negative lumbar puncture result sufficient to rule out subarachnoid hemorrhage? *Ann Emerg Med.*  
821 2008;51:707-713.  
822
- 823 69. Foot C, Staib A. How valuable is a lumbar puncture in the management of patients with suspected  
824 subarachnoid haemorrhage? *Emerg Med.* 2001;13:326-332.  
825
- 826 70. O'Neill J, McLaggan S, Gibson R. Acute headache and subarachnoid haemorrhage: a retrospective  
827 review of CT and lumbar puncture findings. *Scott Med J.* 2005;50:151-153.  
828
- 829 71. Boesiger BM, Shiber JR. Subarachnoid hemorrhage diagnosis by computed tomography and lumbar  
830 puncture: are fifth generation CT scanners better at identifying subarachnoid hemorrhage? *J Emerg Med.*  
831 2005;29:23-27.  
832
- 833 72. Byyny RL, Mower WR, Shum N, et al. Sensitivity of noncontrast cranial computed tomography for the  
834 emergency department diagnosis of subarachnoid hemorrhage. *Ann Emerg Med.* 2008;51:697-703.  
835
- 836 73. Petito F, Plum F. The lumbar puncture. *N Engl J Med.* 1974;290:225-227.  
837
- 838 74. Lashutka MK, Chandra A, Murray HN, et al. The relation of intracranial pressure to intraocular pressure.  
839 *Ann Emerg Med.* 2004;43:585-591.  
840
- 841 75. Schull M. Lumbar puncture first: an alternative model for the investigation of lone acute sudden  
842 headache. *Acad Emerg Med.* 1999;6:131-136.  
843
- 844 76. Duffy GP. Lumbar puncture in the presence of raised intracranial pressure. *BMJ.* 1969;1:407-409.  
845
- 846 77. Duffy GP. Lumbar puncture in spontaneous subarachnoid hemorrhage. *BMJ.* 1982;285:1163-1164.  
847
- 848 78. French JK, Glasgow GL. Lumbar puncture in subarachnoid hemorrhage: yes or no? *N Z Med J.*  
849 1985;98:383-384.  
850
- 851 79. Zisfein J, Tuchman AJ. Risks of lumbar puncture in the presence of intracranial mass lesions. *Mt Sinai J*  
852 *Med.* 1988;55:283-287.  
853
- 854 80. Gopoi AK, Whitehouse JD, Simel DL, et al. Cranial computed tomography before lumbar puncture: a  
855 prospective clinical evaluation. *Arch Intern Med.* 1999;159:2681-2685.  
856
- 857 81. Savitz SI, Edlow J. Thunderclap headache with normal CT and lumbar puncture: further investigations  
858 are unnecessary: for. *Stroke.* 2008;39:1392-1393.  
859
- 860 82. Field A, Wang E. Evaluation of the patient with nontraumatic headache: an evidence-based approach.  
861 *Emerg Med Clin North Am.* 1999;17:127-152.  
862
- 863 83. Walton J. *Subarachnoid Haemorrhage.* Edinburgh, Scotland: E&S Livingstone; 1956.  
864
- 865 84. Raps EC, Rogers JD, Galetta SL, et al. The clinical spectrum of unruptured intracranial aneurysms. *Arch*  
866 *Neurol.* 1993;50:265-268.

- 867  
868 85. Witham TF, Kaufmann AM. Unruptured cerebral aneurysm producing a thunderclap headache. *Am J*  
869 *Emerg Med.* 2000;18:88-90.  
870  
871 86. McCarron MO, Choudhari KA. Aneurysmal subarachnoid leak with normal CT and CSF  
872 spectrophotometry. *Neurology.* 2005;64:923.  
873  
874 87. Hughes RL. Identification and treatment of cerebral aneurysms after sentinel headache. *Neurology.*  
875 1992;42:1118-1119.  
876  
877 88. Slivka A, Philbrook B. Clinical and angiographic features of thunderclap headache. *Headache.*  
878 1995;35:1-6.  
879  
880 89. Dodick DW, Brown RD, Britton JW, et al. Nonaneurysmal thunderclap headache with diffuse, multifocal,  
881 segmental, and reversible vasospasm. *Cephalalgia.* 1999;19:118-123.  
882  
883 90. Carstairs SD, Tanen DA, Duncan TD, et al. Computed tomographic angiography for the evaluation of  
884 aneurysmal subarachnoid hemorrhage. *Acad Emerg Med.* 2006;13:486-492.  
885  
886 91. Sekhar L, Heros R. Origin, growth, and rupture of saccular aneurysm: a review. *Neurosurgery.*  
887 1981;8:248-260.  
888  
889  
890  
891  
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**Evidentiary Table.**

<b>Study</b>	<b>Year</b>	<b>Design</b>	<b>Intervention(s)/Test(s)/Modality</b>	<b>Outcome Measure/Criterion Standard</b>	<b>Results</b>	<b>Limitations/Comments</b>	<b>Class</b>
Goldstein et al <sup>1</sup>	2006	Retrospective case cohort of all US ED headaches	Database query of ED headaches and characteristic of these visits	Testing utilization; demographic trends	Variation in imaging use; age relation to pathology	Follow-up limited; data from ED records	III
Perry et al <sup>3</sup>	2005	Prospective cohort during 2 ½ y period; consecutive patients >15 y of age with a nontraumatic acute headache (onset to peak headache less than 1 h) and normal neurologic examination	Attitudes and judgment of emergency physicians in management of acute headache	Pretest ability of physicians to predict subarachnoid hemorrhage	747 patients enrolled; emergency physicians reported being “uncomfortable” or “very uncomfortable” with performing LP without CT in 49.6% of cases and in 75.4% of cases they were uncomfortable in performing no tests; in only 10.2% of the cases, emergency physicians were “very comfortable” with performing an LP without CT; although emergency physicians were able to discriminate subarachnoid hemorrhage from causes of headache, they were generally not willing to perform an LP without first obtaining a head CT scan	Inclusion criteria allowed less severe headaches to be enrolled by including headaches with slower onset (up to 1 h); although prospective data were completed for historical and physical findings for 747 patients, responses were missing for comfort and predictive questions making only 625 patients for LP question, 659 for no testing, and 639 for pretest probability; lack of standard definition of a positive subarachnoid hemorrhage	II

894 **Evidentiary Table (continued).**

Study	Year	Design	Intervention(s)/Test(s)/Modality	Outcome Measure/Criterion Standard	Results	Limitations/Comments	Class
Seymour et al <sup>10</sup>	1995	Case series	3 cases of patients with intracranial hemorrhage presenting with headache who responded to analgesics	Pain relief/none	These 3 patients had significant relief with ketorolac or prochlorperazine	Design	III
Gross et al <sup>11</sup>	1995	Case series	3 cases of headache patients with inflammatory processes (infectious or carcinomatous meningitis) who responded to analgesics	Pain relief/none	These 3 patients had significant relief with dihydroergotamine or metoclopramide	Design	III
Lipton et al <sup>12</sup>	1997	Case report	1 patient with carbon monoxide poisoning who received sumatriptan	Pain relief/none	Single patient with carbon monoxide poisoning had pain relief with sumatriptan	Design	III
Agostoni <sup>13</sup>	2004	2 case series, 1 prospective, 1 retrospective	Retrospective series of 49 patients with cerebral venous thromboses presenting with headache, some of whom were given analgesics; prospective series of 35 similar patients	Pain relief/none (was not the primary measure in study)	Retrospective: 4/23 patients (who had pain relief recorded) had relief with "common analgesics"; prospective: 1/18 had full relief, 9/18 had partial relief	Design; not a predefined outcome measure, even in the prospective series	III
Abisaab et al <sup>14</sup>	2004	Case report	1 postpartum patient with a bilateral carotid dissection	Pain relief/none	"Immediate" relief with subcutaneous sumatriptan	Design	III
Leira et al <sup>15</sup>	2001	Case report	1 case of spontaneous carotid dissection	Pain relief/none	"90%" relief of pain 2 h after a 50 mg oral dose of sumatriptan	Design	III
Pfadenhauer et al <sup>16</sup>	2006	Case series	3 patients with subarachnoid hemorrhage given sumatriptan	Pain relief/none	2 cases with subcutaneous sumatriptan and 1 with oral sumatriptan; all had partial pain relief	Design	III

895 **Evidentiary Table (continued).**

<b>Study</b>	<b>Year</b>	<b>Design</b>	<b>Intervention(s)/Test(s)/Modality</b>	<b>Outcome Measure/Criterion Standard</b>	<b>Results</b>	<b>Limitations/Comments</b>	<b>Class</b>
Rothrock <sup>17</sup>	2005	Case report	1 case of subarachnoid hemorrhage given sumatriptan	Pain relief/none	1 case with subarachnoid hemorrhage whose pain went from severe to mild after subcutaneous sumatriptan	Design	III
Wang et al <sup>18</sup>	2004	Case series	16 cases of dilated cyst of the cavum septi pellucidi	Pain relief/none	7/16 cases showed a “fair response” to indomethacin	Design	III
US Headache Consortium <sup>22</sup>	2000	Retrospective review of literature from 1966-1998	Review of all English-language studies evaluating neuroimaging in the setting of nonacute headache	Summary recommendations	Recommendations: 1) neuroimaging should be considered in nonacute headache and unexplained neurologic findings (grade B); 2) insufficient evidence about neuroimaging in presence or absence of neurologic symptoms (grade C); 3) neuroimaging usually not warranted in migraine and normal examination (grade B); 4) insufficient evidence in tension-type headache (grade C); 5) insufficient evidence regarding CT or MRI in migraine and nonacute headache (grade C)	Design	III

896 **Evidentiary Table (continued).**

Study	Year	Design	Intervention(s)/Test(s)/Modality	Outcome Measure/Criterion Standard	Results	Limitations/Comments	Class
Lledo et al <sup>24</sup>	1994	1 y prospective study	Inclusion: acute sudden-onset headache with no history, normal neurologic examination by neurologist; all patients had CT, if normal, LP performed; 3 mo follow-up	27 patients enrolled: 9 with subarachnoid hemorrhage, 1 with intraventricular hemorrhage, 1 with bacterial meningitis, 1 with viral meningitis, 15 unknown	No combination of findings identified patients with subarachnoid hemorrhage; CT findings positive in 4/9 patients with subarachnoid hemorrhage; neither altered mental status, neurologic examination, nor improving symptoms distinguished subarachnoid hemorrhage group	No exclusion criteria given; small sample size with no power analysis; patients followed for 3 mo; no angiograms performed to rule out unruptured aneurysm	I
Harling et al <sup>25</sup>	1989	Prospective study of patients with thunderclap headache and normal brain CT and CSF results; of the 49 patients, 35 had subarachnoid hemorrhage	Follow-up at 18 mo	Subarachnoid hemorrhage at 18 mo follow-up; 8/14 had angiograms (all results negative)	Of the 14 patients with a negative initial evaluation, none had subarachnoid hemorrhage or sudden death at follow-up	Selection bias; small numbers; inclusion criteria not defined; not all patients had angiogram	III
Akpek et al <sup>26</sup>	1995	Retrospective study	CT imaging in headache; inclusion: no neurologic findings; exclusion: complaints of vision change, vertigo, dizziness, personality change, cancer	Cost-effectiveness of CT imaging in headache patients	592 patients (8-88 y); no patient with acute intracranial process was identified	Retrospective design; no formal neurologic examination; all exclusion criteria not reported	II

897 **Evidentiary Table (continued).**

Study	Year	Design	Intervention(s)/Test(s)/Modality	Outcome Measure/Criterion Standard	Results	Limitations/Comments	Class
Demaerel et al <sup>27</sup>	1996	Prospective series	363 consecutive patients with chronic headache referred to radiology for CT with/without contrast; inclusion: normal neurologic examination; exclusion: vertigo, dizziness, migraine, epilepsy	Sensitivity of CT imaging in chronic headache population with normal neurologic examination	11 (3%) had a space-occupying lesion; none required emergency surgery	Did not evaluate acute headache population; selection bias	III
Mitchell et al <sup>28</sup>	1993	Prospective study of military ED and clinics	CT imaging in the headache patient; inclusion: headache of undetermined origin; exclusion: seizure, trauma, neoplasms, known etiology of headache	CT imaging sensitivity to detect significant intracranial findings	350 patients; 7 (2%) had significant findings (eg, tumor, subdural hematoma, subarachnoid hemorrhage, hydrocephalus, sinusitis); 27 had abnormal examination but normal CT imaging result; all patients with positive CT findings had abnormal physical or neurologic examination; 27 reported "worst headache of life"; only 1 had subarachnoid hemorrhage; unusual symptomatology (eg, "worst headache," syncope, vomiting) did not predict positive CT findings on examination	Study performed by radiology; no protocol for referral; selection bias; although consecutive patients were referred from ED and clinics, it does not necessarily represent consecutive patients who presented to ED or clinics with headache	II

898 **Evidentiary Table (continued).**

Study	Year	Design	Intervention(s)/Test(s)/Modality	Outcome Measure/Criterion Standard	Results	Limitations/Comments	Class
Mills et al <sup>29</sup>	1986	Prospective observational	ED patients having urgent CT imaging	Results of CT imaging in ED patient population	42 patients in headache subset (407 total patients); 21% had positive CT finding; only 1 patient had focal examination; 29% with "worst headache of life" had positive CT result (LP not provided)	Selection bias-enrollment dependent on house staff; neurologic examination by emergency medicine house staff; trauma patients included but percentage not reported	III
Ramirez-Lassepas et al <sup>30</sup>	1997	Retrospective review	15-mo review of patients with complaint of headache; random selection of 329 of 1,720 ED patients and 139 of hospitalized patients; 6 mo follow-up	4.2% ED patients evaluated for headache (1,859/44,080); 139 hospitalized; 3.8% had intracranial process (subarachnoid hemorrhage, tumor, intracranial hemorrhage, bacterial meningitis, cerebral infarction, herpes encephalitis)	Clinical findings and historical findings had a low positive predictive value but absence had a high negative predictive value; no association found between type of headache and pathologic entities; abnormal neurologic examination and headache had a 39% positive predictive value for intracranial process; acute onset, occipitounuchal location, and age older than 55 y were identified as clinical parameters associated with intracranial process	Selection process and inclusion/exclusion criteria not well described; no patient follow-up of patients discharged from ED; randomization process not described; hospitalized patients not described	II

899 **Evidentiary Table (continued).**

Study	Year	Design	Intervention(s)/Test(s)/Modality	Outcome Measure/Criterion Standard	Results	Limitations/Comments	Class
Kahn et al <sup>31</sup>	1993	Retrospective review	Comparison of CT imaging for nontraumatic headache in 2 centers in United States and Canada; inclusion: acute migraine or headache; exclusion: trauma or surgery	1,111 CT imaging examinations during 3-y period; 11% had acute intracranial process (eg, hemorrhage, infarction, tumor); 18% had chronic process (eg, old infarction, atrophy)	Study does not specifically address predictors of positive findings because population not well described; frequency highest in hospitalized patients and those >40 y; proportion of positive findings in migraine group did not differ from other group	Did not provide clinical information that determined testing	III
Duarte et al <sup>32</sup>	1996	Prospective study	100 consecutive patients with new headache occurring within 1 y of presentation; recruited from general practitioners; all patients had CT with/without contrast; all patients >60 y had erythrocyte sedimentation rate	Prevalence of abnormal CT imaging findings in patients referred for new-onset headache	Although the study identified a large number of patients with intracranial process, it failed to identify those patients in need of imaging study in the ED; 80 patients had normal examination findings; 21 had intracranial neoplasms (13 with normal neurologic examinations); no combination of historical or physical findings excluded headache patients with intracranial process	Recruitment procedure biased, referral-population not necessarily reflective of ED population; not specifically dealing with acute headache	II

900 **Evidentiary Table (continued).**

Study	Year	Design	Intervention(s)/Test(s)/Modality	Outcome Measure/Criterion Standard	Results	Limitations/Comments	Class
Day and Raskin <sup>33</sup>	1986	Case report	Angiography in a patient with thunderclap headache and normal brain CT and CSF results	Symptom relief after aneurysm surgery	1 patient who had an aneurysm and diffuse vasospasm; the aneurysm was clipped; symptoms resolved	Single patient in whom symptoms may not have been related to the aneurysm	III
Linn et al <sup>35</sup>	1994	Prospective cohort series of patients with thunderclap headache, and normal brain CT and CSF	103 patients with thunderclap headache seen by Dutch general practitioners; 11% had subarachnoid hemorrhage; those with negative initial evaluations were followed for 1 y	No subarachnoid hemorrhage or sudden death at 1-y clinical follow-up	No patient not identified in the initial evaluation had subarachnoid hemorrhage or sudden death	Not all patients had a standard diagnostic evaluation (not all had CT); given study setting, may have limited external validity	II
Wijdicks et al <sup>36</sup>	1988	Retrospective analysis of a prospectively collected series of patients with thunderclap headache and normal brain CT and CSF results	Follow-up of patients for evidence of subarachnoid hemorrhage or sudden unexplained death; 6/71 had negative angiograms; none of the patients had subarachnoid hemorrhage	No subarachnoid hemorrhage or sudden death at (average) 3.3-y follow-up	No patient had subarachnoid hemorrhage or sudden death at follow-up	Design; nonstandard evaluation	III

901 **Evidentiary Table (continued).**

<b>Study</b>	<b>Year</b>	<b>Design</b>	<b>Intervention(s)/Test(s)/ Modality</b>	<b>Outcome Measure/Criterion Standard</b>	<b>Results</b>	<b>Limitations/Comments</b>	<b>Class</b>
Landtblom et al <sup>37</sup>	2002	Prospective cohort series of patients with thunderclap headache and normal brain CT and CSF results	Study with 2 phases: Phase 1: 31 mo during which neurologist on call; Phase 2: 19 mo during which there was better coverage for incidence study	No subarachnoid hemorrhage or sudden death at 1-y clinical follow-up	No patient with a negative CT and CSF analysis at the first visit was later found to have subarachnoid hemorrhage at 12 mo follow-up	All patients examined by study neurologists; given study setting, may have limited external validity	II
DeLashaw et al <sup>45</sup>	2005	Case review	Presentation of a single case of postpartum CVT and review of identification, management, and treatment	Case review	Review	Design	III
English and Mulvey <sup>46</sup>	2004	Case report	Report of arteriovenous malformation bleed in woman during induction of labor	Case report	Review	Design	III

902 **Evidentiary Table (continued).**

<b>Study</b>	<b>Year</b>	<b>Design</b>	<b>Intervention(s)/Test(s)/ Modality</b>	<b>Outcome Measure/Criterion Standard</b>	<b>Results</b>	<b>Limitations/Comments</b>	<b>Class</b>
Sidman et al <sup>60</sup>	1996	Retrospective review	Reviewed all ED patients receiving third generation CT and LP for nontraumatic subarachnoid hemorrhage	140 patients identified with subarachnoid hemorrhage; sensitivity of CT in the diagnosis of nontraumatic subarachnoid hemorrhage when performed $\leq 12$ h of symptom duration was 100% (80/80), and was 81.7% (49/60) after 12 h of symptom duration (95% CI 95%-100% and 69.5%-90.4%, respectively; $P < 0.0001$ ); 11/140 had a negative CT and positive spinal fluid analysis, yielding an overall sensitivity of 92.1% (129/140)	Review	Design	III
Shah et al <sup>63</sup>	2003	Retrospective review	Reviewed all LP results (N=786) in hospital in attempt to describe traumatic attempt incidence	Incidence of traumatic taps	15% traumatic incidence; better rates in ED	Design	III

903 **Evidentiary Table (continued).**

Study	Year	Design	Intervention(s)/Test(s)/Modality	Outcome Measure/ Criterion Standard	Results	Limitations/Comments	Class
Perry et al <sup>68</sup>	2008	Prospective cohort study of alert patients presenting to 2 tertiary EDs with a chief complaint of nontraumatic headache	592 patients (61 with subarachnoid hemorrhage) in a study to test the accuracy of the diagnostic strategy of combined CT and LP to rule out a subarachnoid hemorrhage	Patients diagnosed with subarachnoid hemorrhage and patients with negative evaluation who did not have subarachnoid hemorrhage on follow-up	All 61 patients with subarachnoid hemorrhage were found by the combined diagnostic strategy: CT (55 patients) or LP (6 patients)	Unable to follow up 20% of patients (though strict measures were taken that make it unlikely those patients had a subsequent subarachnoid hemorrhage); 1 patient later was found to have an asymptomatic aneurysm not thought to have caused the original headache	II
Foot and Staib <sup>69</sup>	2001	Retrospective case review	Reviewed all cases with subarachnoid hemorrhage–type symptoms who had CT and LP	Role of CSF xanthochromia to alter outcome and management	Only 1/189 had CT/LP positive but significant variation on how LP interpreted within their institution	Retrospective; criteria for study entry were LP and having CT; some may have just had CT, which could miss cases; considerable management variation within institution, generalizability questioned	III
O’Neill et al <sup>70</sup>	2005	Retrospective study of acute headache patients presenting to an ED and for whom a brain CT scan was performed	127 patients identified of whom 11 were excluded because of incomplete record retrieval; 19 patients had subarachnoid hemorrhage	Patients diagnosed with subarachnoid hemorrhage by CT scan versus LP	Of the 116 included patients, 81 had a normal CT; 40 of those patients (49%) had LP performed; 6 patients had xanthochromia, all of whom had angiography; 4 were normal; 2 showed aneurysms	Half of eligible patients for LP did not have LPs done; half of patients had no diagnosis on discharge	III

904 **Evidentiary Table (continued).**

Study	Year	Design	Intervention(s)/Test(s)/Modality	Outcome Measure/ Criterion Standard	Results	Limitations/Comments	Class
Boesiger and Shiber <sup>71</sup>	2005	Retrospective chart review	Identified ED headache patients having both CT (fifth generation) and LP to estimate local imaging sensitivity and specificity for subarachnoid hemorrhage	Disagreement between CT and LP	N=177; no missed subarachnoid hemorrhage cases in CT-negative patients; suggests newer CT imaging more sensitive than earlier scanners	Retrospective review; selection bias (CT but patient refused LP); missed cases	III
Bynny et al <sup>72</sup>	2008	Retrospective chart review	149 patients presenting to or transferred to an ED with nontraumatic subarachnoid hemorrhage to find CT sensitivity; 4-slice, 4-detector CT scanner was used	Percentage of patients whose CT scans were negative but who were diagnosed with LP	139/149 patients with nontraumatic subarachnoid hemorrhage had positive CT scan results; 10/149 were diagnosed by LP; in less severely affected patients (normal mental status) 78/87 patients had a positive CT result (sensitivity of 90%)	Referral tertiary care population; some patients with missing LP data	III
Duffy <sup>76</sup>	1969	This appears to be a retrospective review of patients found to have midbrain and medullary compression syndromes after an LP	LP	Midbrain and medullary compression syndrome	10 of 30 patients stopped breathing or developed unequal pupils while the needle was still in place or shortly after it was removed; 15 of the 30 patients had marked deterioration within 24 h of the procedure; 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 radiograph results	Study design not described; no analysis for bias selection addressed; LP in patients with no complications not included; the relative contributions of the LP versus the natural disease course to the patient's clinical deterioration is not known	X

905 **Evidentiary Table (continued).**

Study	Year	Design	Intervention(s)/Test(s)/Modality	Outcome Measure/Criterion Standard	Results	Limitations/Comments	Class
Duffy <sup>77</sup>	1982	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	LP	LP complication while spinal needle is in place	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; conclusion: the risk of herniation is significant in patients who undergo spinal tap and have an intracranial hematoma with a hemispheric shift	Unclear study design; there was no standardization in the management of these patients; LP in patients with no neurologic signs were not included	III

906 **Evidentiary Table (continued).**

Study	Year	Design	Intervention(s)/Test(s)/Modality	Outcome Measure/Criterion Standard	Results	Limitations/Comments	Class
French and Glasgow <sup>78</sup>	1985	Retrospective chart review of 109 patients admitted for subarachnoid hemorrhage; inclusion: patients who were drowsy, confused, or had “mild” hemiparesis; exclusion: stupor, coma, or “significant” hemiparesis	Lumbar puncture	Mild hemiparesis, drowsiness, confusion	One of the 70 patients, a patient with subarachnoid hemorrhage deteriorated after the LP and died after 12 days, leading to the conclusion that herniation, even in the neurologically symptomatic patient, is uncommon	Retrospective study design; timing of CT scans was not reported; no long-term outcome data reported	III

907 **Evidentiary Table (continued).**

Study	Year	Design	Intervention(s)/Test(s)/Modality	Outcome Measure/Criterion Standard	Results	Limitations/Comments	Class
Zisfein and Tuchman <sup>79</sup>	1988	Prospective observational design during a 3-y period; inclusion: patients requiring a LP to rule out meningitis who subsequent to procedure, are found within 1 wk 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	LP	Neurologic deterioration in patients receiving LP	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 at 48 h after the LP; 1 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; herniation is uncommon in the setting of intracranial mass lesions even in the presence of mass effect	Indications for suspicion of meningitis are not reported; without a prespinal tap CT scan there is no way to know whether the shift on CT scan resulted from the LP; no patients suspect of having subarachnoid hemorrhage are included; heterogeneous group of CNS lesions	III

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917 **Evidentiary Table (continued).**

Study	Year	Design	Intervention(s)/Test(s)/Modality	Outcome Measure/Criterion Standard	Results	Limitations/Comments	Class
Gopol et al <sup>80</sup>	1999	Prospective cohort during an 18-mo period	Preselected medical history and physical examination data were collected on all patients who were determined to need a LP; internal medicine resident (with ED attending supervision) suspicion that a patient would have a CT finding that would contraindicate LP was also documented before performance of the CT scan	Physician pretest ability to predict the likelihood of a CT finding that would contraindicate dural puncture	111 patients were assessed; reasons for LP: rule out subarachnoid hemorrhage (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; 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	Heterogeneous patient population; small number of patients with disease	II

918 **Evidentiary Table (continued).**

Study	Year	Design	Intervention(s)/Test(s)/Modality	Outcome Measure/Criterion Standard	Results	Limitations/Comments	Class
Raps et al <sup>84</sup>	1993	Retrospective chart review of patients presenting to a tertiary care center with unruptured intracranial aneurysm	54 of 111 patients had acute symptoms; 7 presented with a thunderclap headache; all had at least transient neurologic deficits	Symptoms thought to be due to unruptured aneurysms	7 patients presented with an acute severe headache probably related to the unruptured aneurysm	Study design; selection bias (tertiary referral center)	III
Witham and Kaufmann <sup>85</sup>	2000	Case report	1 patient with a 13 mm unruptured aneurysm with normal CT and a traumatic LP	Findings at surgery	Single case of patient with symptomatic aneurysm and normal CT result but a traumatic LP (high RBC count with no xanthochromia)	Design	III
McCarron and Choudhari <sup>86</sup>	2005	Case report	Surgery in a patient with thunderclap headache with negative findings on standard work-up	Findings at surgery	Single case of patient with symptomatic aneurysm and negative CT and LP results	Design; CSF not tested until 7 days after onset of headache	III
Hughes <sup>87</sup>	1992	2 case reports	2 patients with thunderclap headache and negative CT findings (1 who also had negative LP findings)	Findings at angiography 2 wk after onset of headache	2 cases of (symptomatic but unruptured) aneurysm found after negative evaluations	Design	III
Carstairs et al <sup>90</sup>	2006	Prospective cohort series	116 patients with thunderclap headache enrolled, 106 completed the study	Findings on digital angiogram	6 of the 116 patients had aneurysms by CT angiography	Aneurysms found could have been incidental; 3 of the 6 had abnormal CT or LP results; 1 other was a false positive (had negative formal angiogram)	II

919 *CI*, confidence interval; *CNS*, central nervous system; *CSF*, cerebrospinal fluid; *CT*, computed tomography; *CVT*, cerebral venous thrombosis; *ED*, emergency  
920 department; *h*, hour; *LP*, lumbar puncture; *mg*, milligram; *mm*, millimeter; *mo*, month; *MRI*, magnetic resonance imaging; *RBC*, red blood cell; *US*, United  
921 States; *wk*, week; *y*, year.

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924**Appendix A.** Literature classification schema.\*

<b>Design/ Class</b>	<b>Therapy<sup>†</sup></b>	<b>Diagnosis<sup>‡</sup></b>	<b>Prognosis<sup>§</sup></b>
1	Randomized, controlled trial or meta-analyses of randomized trials	Prospective cohort using a criterion standard	Population prospective cohort
2	Nonrandomized trial	Retrospective observational	Retrospective cohort Case control
3	Case series Case report Other (eg, consensus, review)	Case series Case report Other (eg, consensus, review)	Case series Case report Other (eg, consensus, review)

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\*Some designs (eg, surveys) will not fit this schema and should be assessed individually.

<sup>†</sup>Objective is to measure therapeutic efficacy comparing  $\geq 2$  interventions.<sup>‡</sup>Objective is to determine the sensitivity and specificity of diagnostic tests.<sup>§</sup>Objective is to predict outcome including mortality and morbidity.933  
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937**Appendix B.** Approach to downgrading strength of evidence.938  
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<b>Downgrading</b>	<b>Design/Class</b>		
	<b>1</b>	<b>2</b>	<b>3</b>
None	I	II	III
1 level	II	III	X
2 levels	III	X	X
Fatally flawed	X	X	X