Headaches are common complaints in the emergency department, but the causes of secondary headaches are often misdiagnosed. The authors review what to stay alert for in the history and physical examination, what tests to order, and what diagnoses physicians cannot afford to miss.

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Headaches—from both primary and secondary causes—are common complaints that account for 1% to 4% of all emergency department visits. Most headaches have benign causes. For example, primary headaches, including migraine, cluster, and tension headaches, are not associated with pathology. Secondary headaches, however, are due to underlying disorders that can be limb-, vision-, brain-, or life-threatening. Approximately 4% to 14% of all headaches fall into this category.

Diagnosing the cause of secondary headaches can challenge the most seasoned physician. For example, only about 1% of patients presenting to the emergency department with a headache have a subarachnoid hemorrhage, so physicians regularly misdiagnose these patients. On the other hand, other types of secondary headaches, such as those that are sinus- and fever-related, are more common and easier to diagnose. Migraine headaches are very common in the general population, with a one-year incidence of about 11% and a lifetime incidence of about 18%. Even so, differentiating between primary and secondary headaches can be difficult. Unfortunately, a delay in diagnosing a serious secondary cause of headache is a common reason for malpractice litigation in emergency medicine.

Why is differentiating between primary and secondary causes of headache so challenging? One reason is because the pathology of all headaches follows a common final pathway. Various stimuli in the brain, including the stretching of intracranial vessels, increased intracranial pressure (ICP), and meningeal irritation, activate trigeminal afferent C fibers, triggering a cascade of inflammatory reactions that result in the transmission of pain. Therefore, a favorable response to analgesics does not necessarily mean a headache has a benign cause.

The International Headache Society has devised a method for categorizing primary and secondary headaches. However, the emergency physician’s goal is not necessarily to arrive at an exact diagnosis immediately, but rather to help treat the pain and rule out potentially catastrophic causes, such as subarachnoid hemorrhage, meningitis, or stroke. With this in mind, it may be more helpful to divide headaches into two groups: those that are benign and those with “cannot miss” causes (see box below).
KEY HISTORY QUESTIONS

The best way to differentiate between benign and serious causes of headache is with a complete history and physical examination. Because most headaches are benign, many patients may be safely discharged home with appropriate follow-up care. However, some may need other diagnostic tests, such as imaging and lumbar puncture.

History-taking should be based on the standard questions for any patient with pain, so ask about onset, quality, severity, timing, and associated symptoms, as well as any relevant medical, social, or family history.

Onset of the headache. An abrupt onset or “thunderclap” headache raises a red flag because it suggests intracranial hemorrhage, thrombosis of an unruptured aneurysm, or cerebral venous sinus thrombosis (CVST). An acute onset of headache in patients older than 55 is associated with a greater likelihood of intracranial pathology. The patient’s activity at the onset of the headache may help in diagnosing exertional or postcoital headache, but other serious causes of abrupt onset of headache must still be ruled out. In one study, subarachnoid hemorrhage occurred in 11.8% of people during sleep or rest.

Quality of the headache. Many patients with sentinel bleeds will describe a qualitatively different headache. For example, they may say their headache pain is usually throbbing but is now sharp or stabbing. Any headache that is different than normal for a patient warrants a work-up for subarachnoid hemorrhage.

Severity of the headache. Physicians are rightly concerned when a patient describes a headache as “the worst in my life,” yet two studies found that most of these patients had benign causes of headache. In addition, headaches from subarachnoid hemorrhage can improve spontaneously with simple analgesics. But even if the patient reports improvement with these drugs, patients whose headaches increase in severity should be evaluated for subarachnoid hemorrhage.

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**“Cannot Miss” Causes of Headache**

- meningitis or encephalitis
- subarachnoid hemorrhage
- stroke
- cervical artery dissection
- hypertensive encephalopathy
- idiopathic intracranial hypertension
- temporal arteritis
- acute angle-closure glaucoma
- intracranial mass
- cerebral venous sinus thrombosis
- carbon monoxide poisoning
- pituitary apoplexy

Source: Adapted from Edlow JA (see Suggested Reading).
Timing of the headache. Chronic daily headaches or short, jabbing headaches lasting only a few seconds are usually benign, whereas acute headaches or those that increase over time may have serious causes. Symptoms such as nausea and vomiting can occur with migraines, but they can also occur with tumors or intracranial hemorrhage. This fact reinforces the importance of comparing the current headache to the patient’s past headaches. A currently vomiting patient with a history of migraines that haven’t caused vomiting before needs a more thorough work-up than a patient who always vomits with migraines.

Associated symptoms. Visual changes such as diplopia may occur with ocular migraines but can also be caused by a third-nerve palsy from an aneurysm or mass or a sixth-nerve palsy from increased or decreased ICP. Other focal neurologic symptoms, including seizures, should prompt further evaluation.

Medical, social, and family history. A history of hypertension or coronary artery disease suggests a hypertensive encephalopathy or vascular cause such as stroke. A history of a hypercoagulable state or inflammatory bowel disease suggests CVST. Patients who are immunocompromised are at higher risk for secondary causes of headache, including infection and mass. A family history of aneurysm or glaucoma raises red flags for leaking aneurysm or acute-angle glaucoma. In addition, chronic headaches in the winter should raise concern for carbon monoxide (CO) poisoning.

IMPORTANT OF THE NEUROLOGIC EXAM

Physical examination findings can also pinpoint which patients need further evaluation for headache. General appearance may reveal patients who have photophobia or altered mental status. Vital signs may include an elevated temperature, suggesting an infectious etiology. Heart rate and blood pressure are less reliable because they may be altered by pain or stress.

When evaluating headache, the neurologic examination is the most important aspect of the physical exam. One study found that an abnormal neurologic exam was the best clinical predictor of intracranial pathology. Any patient with headache who has a newly abnormal neurologic exam or altered mental status warrants further evaluation (see box below), with the exception of those who have a well-documented history of migraine with auras. Mental status should be evaluated because an acute change could indicate meningitis or encephalitis, CO poisoning, or a mass causing increased ICP.
Cranial nerve testing may demonstrate a third-nerve palsy from subarachnoid hemorrhage or cavernous sinus thrombosis or a sixth-nerve palsy from increased ICP (see table below). Fundi must be examined for loss of venous pulsation or papilledema suggesting increased ICP. Visual fields should also be examined because a visual field cut can be seen in pituitary apoplexy, mass, and stroke. Decreased visual acuity with a headache is a sign of temporal arteritis or acute angle-closure glaucoma. The combination of ptosis and meiosis with neck pain raises concern for cervical artery dissection. Once the cranial nerves are assessed, the remainder of the neurologic exam should be completed, with attention to unilateral weakness or abnormal gait, which may signal a subcortical or cerebellar stroke.

### Cranial Nerve Findings in Secondary Causes of Headache

<table>
<thead>
<tr>
<th>Finding</th>
<th>Diagnosis</th>
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<tr>
<td>third-nerve palsy</td>
<td>subarachnoid hemorrhage, cavernous venous thrombosis</td>
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<tr>
<td>sixth-nerve palsy</td>
<td>conditions associated with increased intracranial pressure mass, stroke, pituitary apoplexy</td>
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<tr>
<td>visual field cut</td>
<td>temporal arteritis, acute narrow-angle glaucoma carotid artery dissection</td>
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<tr>
<td>decreased visual acuity</td>
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<td>partial Horner syndrome</td>
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Source: Adapted from Eikelbier (J.A. see Suggested Reading).

### Worrisome Factors for Secondary Causes of Headache

- New onset after age 50
- New neurologic abnormalities or altered mental status
- Immunocompromised patient
- Patient with history of cancer
- Associated symptoms:
  - Fever
  - Nausea, vomiting
  - Visual disturbances
  - Seizures, syncope
  - Cognitive disturbances
- Trauma
- Changes in existing headache pattern:
  - Increasing frequency
  - Increasing severity

Other physical examination findings that may help diagnose the cause of headache may be found by examining the head, ears, eyes, nose, and throat. Vesicles on the scalp or tip of the nose suggest herpes zoster, whereas vesicles in the external ear suggest Ramsay Hunt syndrome. A red, painful eye should be evaluated for acute angle-closure glaucoma by measuring the ocular
pressure. Temporal artery tenderness can be seen with temporal arteritis. A proptotic eye with chemosis can occur with cavernous sinus thrombosis. Other examination findings, including the Kernig and Brudzinski signs, may be helpful, but one review found that only the jolt accentuation of a headache was sensitive for the diagnosis of meningitis.

DIAGNOSTIC STUDIES

If the patient has new neurologic abnormalities, cognitive disturbances, or other serious problems, the next step is to obtain a noncontrast cranial computed tomography (CT) scan. However, keep in mind that the scan has the following limitations:

- The sensitivity of the test decays rapidly from the initial onset of symptoms. In the International Cooperative Study on the Timing of Aneurysm Surgery, 92% of the scans were positive on the day of rupture, but only 86% were positive one day later and only 58% five days later.
- Alert patients with less severe symptoms from smaller bleeds will seek care later, so they are more likely to have normal CT scans.
- Errors in interpretation can occur, especially in patients with small volume bleeds.
- Technique is crucial. Thicker cuts of 10 mm will miss small volumes of blood, so 3-mm cuts are recommended.
- Hyperdense blood on a CT scan is dependent on the hematocrit level, so patients with a hematocrit of less than 30 may appear to have a negative scan.
- In rare cases, false positive results may occur in patients with purulent meningitis and intravenous contrast neurotoxicity.

Physicians must understand these limitations, so that they can warn patients with a suspected subarachnoid hemorrhage that a lumbar puncture may be necessary if the CT scan is negative or equivocal. A lumbar puncture may also identify a patient with atypical meningitis. In addition, physicians should tell patients that other tests, such as magnetic resonance imaging (MRI) or CT angiography, may also be necessary to diagnose the cause of their headaches.

During a lumbar puncture, the opening pressure should be measured. An elevated opening pressure suggests idiopathic intracranial hypertension or CVST. Measuring the opening pressure can also help distinguish between a traumatic tap and a true subarachnoid hemorrhage, which will often cause an elevated pressure. Limitations exist in the analysis of the cerebrospinal fluid (CSF). After intracranial hemorrhage, red cells will eventually be lysed and hemoglobin degraded into oxyhemoglobin and bilirubin, creating xanthochromia. Oxyhemoglobin will be present within a few hours after the bleed, but bilirubin may not be detected for up to 12 hours. Therefore, xanthochromia may not be obvious on spectrophotometry in the early hours following a subarachnoid hemorrhage. That being said, any patient with a persistently bloody tap or xanthochromia (by any method), or both, should have further vascular imaging to rule out subarachnoid hemorrhage.

Other diagnostic studies may be warranted, depending on the physician’s clinical suspicion. Magnetic resonance imaging is superior to CT scanning for diagnosing vascular or neoplastic lesions and pathology in the posterior fossa, so patients with symptoms of stroke or those with focal neurologic findings but negative work-ups should have an MRI. Magnetic resonance
angiography (MRA) can be used to diagnose cervical artery dissection, aneurysms, and CVST. Computed tomography angiography has been shown to be equally sensitive for diagnosing dissection and intracranial aneurysms (although it is not as sensitive for diagnosing CVST) and is more readily available to most emergency physicians. Other tests such as tonometry can evaluate for increased intraocular pressures in acute angle-closure glaucoma.

The final steps in the diagnosis are neurologic or neurosurgical consultations if the findings are positive or close outpatient follow-up if the findings are negative.

MOST COMMON SERIOUS CAUSES

Among the most common serious causes of headaches that physicians cannot afford to misdiagnose are subarachnoid hemorrhage, cervical artery dissection, CO poisoning, hypertensive encephalopathy, temporal arteritis, and acute narrow-angle glaucoma.

Subarachnoid hemorrhage. Despite the widespread availability of CT scans, subarachnoid hemorrhage is still misdiagnosed on the first visit in a significant percentage of patients, although this number seems to be decreasing. Even if both the CT scan and lumbar puncture are negative, an occasional patient will have a symptomatic aneurysm. In a retrospective study over 3.3 years of 71 patients who had work-ups for subarachnoid hemorrhage but had negative CT scans and lumbar punctures, no subsequent deaths or subarachnoid hemorrhage occurred. In addition, four prospective studies of 54 patients with normal CT scans and CSF found no sudden death or subarachnoid hemorrhage at a one-year follow-up.

Consider further vascular imaging and neurologic consultation in patients with a very high pre-test probability of subarachnoid hemorrhage, in patients who present longer than two weeks after initial symptoms, in patients who have significant ambiguity in their CT scans or interpretation of their CSF, or in patients whose CSF is unattainable. Physicians should strongly consider transferring patients with subarachnoid hemorrhage to a specialized center with a neurologic critical care unit for further imaging and possible surgery.

Cervical artery dissection. Cervical artery dissection may present with only pain. In fact, one study found that 8% of patients had pain as their only symptom. The nature of the pain is variable, ranging from thunderclap to gradual and progressive to intermittent. Pain may localize to the neck or head, or both. It may be unilateral or bilateral and is almost always different from previous headaches. Given the variable presentation of cervical artery dissection, there is often a delay in the correct diagnosis.

Carotid and vertebral artery dissection will present with different symptoms based on the area of ischemia in the brainstem or cerebellum. Carotid artery dissection may present with neck pain and ophthalmologic findings, including a partial Horner syndrome, monocular transient vision loss, and palsy of the oculomotor nerve. Vertebral artery dissection may present with an occipital headache, vertigo, ipsilateral facial dysesthesia, and nausea and vomiting. Although conventional angiography is the gold standard for diagnosis, MRI or MRA is the preferred method because it is noninvasive. Computed tomography angiography also can be useful.
Carbon monoxide poisoning. The signs and symptoms of CO poisoning are variable and nonspecific. It often occurs in the winter months and in clusters of cases. Patients may present with flu-like symptoms of a severity roughly proportional to their CO-hemoglobin levels. The oxygen saturation is often falsely normal because the dissolved oxygen in the serum is not affected by the CO. The CO-hemoglobin level must be measured directly. Treatment with hyperbaric oxygen is still controversial. Some argue that hyperbaric oxygen protects against neurologic sequelae but this has not been proved. Currently, hyperbaric oxygen therapy is recommended for those with moderate to severe CO poisoning, although this has yet to be defined. There is no firm evidence regarding exactly which patients require treatment, but most experts would advise treating those with loss of consciousness, severe acidosis, neurologic symptoms, cardiac dysfunction, pregnancy, and elevated CO-hemoglobin levels.

Hypertensive encephalopathy. This condition is marked by severe hypertension with altered mental status, papilledema, and evidence of acute end-organ damage. It often occurs in usually normotensive patients who have an acute rise in blood pressure, such as women with eclampsia. Laboratory tests, ECG, urine analysis, and cranial CT scan should be performed. During management, remember that control of cerebral blood flow is based on autoregulation—cerebral blood flow remains constant over a wide range of blood pressures. The treatment goal is reduction of mean arterial pressure by no more than 20% to 25% over a few hours using titratable drugs like nitroprusside and taking care to avoid rapid or severe drops in blood pressure.

Temporal arteritis. This inflammatory disorder may cause a gradual onset of headache. It typically occurs in patients older than age 50; symptoms include headache, jaw claudication, scalp tenderness, and proximal muscle weakness. One study of 254 patients found that 80% had a firm, tender, nonpulsatile cranial artery, which increased the likelihood of an ischemic manifestation. Major complications include monocular blindness and stroke. Diagnosis is made by an elevated erythrocyte sedimentation rate and temporal artery biopsy. High-dose corticosteroids should be started immediately and surgical and ophthalmologic consultations should be obtained for biopsy and an eye examination, respectively.

Acute narrow-angle glaucoma. This disease occurs in only 0.07% of individuals in the general population, so it is often misdiagnosed. One study found that it occurred in patients in their 50s, that headaches were often intermittent, lasting from one to four hours, and that only 36% of patients had visual symptoms. The diagnosis requires a detailed slit-lamp examination and tonometry. Although rare, acute narrow-angle glaucoma should be considered in patients over age 50 who have intermittent headaches.

THE HEADACHE CHALLENGE

Most headaches have benign causes, but the diagnosis of secondary headaches that are limb-, vision-, brain, or life-threatening can challenge the most seasoned emergency physician. The history and physical examination findings determine who needs further evaluation and who can be sent home safely with appropriate follow-up care. Key symptoms and physical examination findings suggestive of “cannot miss” diagnoses help in the successful evaluation of patients with
headaches. By using all three tools—clinical evaluation, brain imaging, and lumbar puncture—physicians can effectively and safely manage patients with secondary headaches.

Suggested Reading


