Subarachnoid Hemorrhage: State of the Art(ery)

David M. Lemonick, MD, FAAEP, FACEP

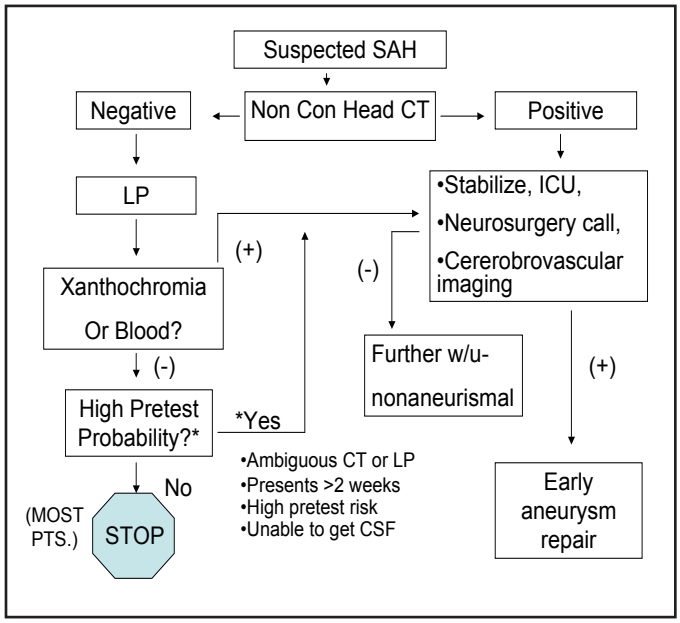
Abstract

Headache is a common chief complaint in primary and ambulatory care settings. The etiology of headache is usually benign, its workup is often minimal and straightforward, and the clinical approach focuses primarily on symptom control. A small proportion of headaches is caused by subarachnoid hemorrhage (SAH), most of which are due to ruptured cerebral aneurysms. Such hemorrhage carries a high mortality, with significant rates of devastating disability among survivors. Misdiagnosis of SAH is frequent and results in medicolegal risk to the unwary physician. An organized, algorithmic approach emphasizes high risk historical and physical examination features that suggest SAH. Expeditious neuroimaging and lumbar puncture are employed to confirm suspected SAH. Diagnosis of SAH requires immediate stabilization, followed by neurosurgical consultation for definitive management. Transfer to high-volume neurosurgical and endovascular centers is associated with improved outcomes for SAH.

Introduction

Headache is a common chief complaint in the emergency department (ED), constituting approximately 2% of all visits. Of these patients, about 1% will have subarachnoid hemorrhage (SAH).[1, 2] In the subset of patients who present with a severe, sudden onset, or "thunderclap," headache and a normal neurologic examination, 10% to 16% will have SAH.[3-8] Thus, emergency physicians see only one subarachnoid hemorrhage out of every 100 headache patients. Further, it is estimated that 5-15% of these are initially misdiagnosed.[9-13] Delayed diagnosis of SAH confers worse outcomes, highlighting the importance of early recognition and treatment.[14] The mortality of SAH is approximately 40%, with another 30% surviving with significant neurological disability.[15] Misdiagnosis of SAH is an important cause of medico-legal actions against physicians.[5,7,9-13,15-18]

Figure 1: Algorithm for workup of suspected SAH

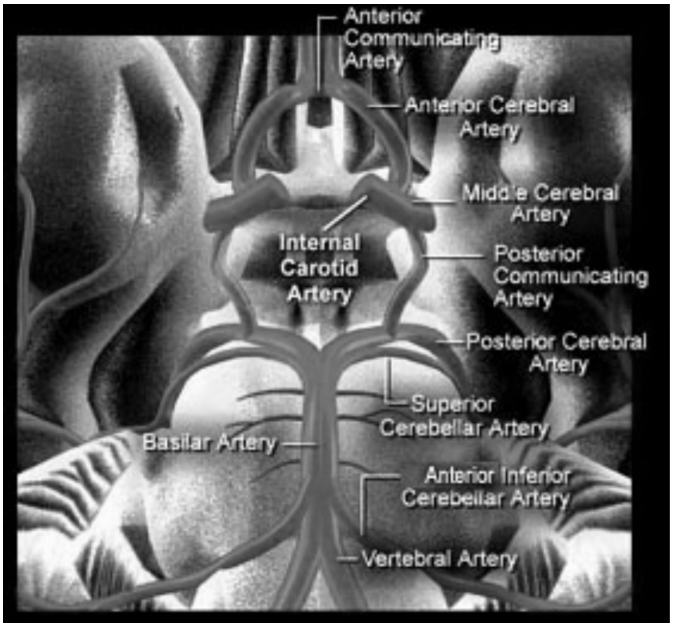


At the same time, an extensive workup of every headache patient in the ED is neither practical nor necessary. Because the diagnosis of SAH will not be made if it is not considered, deciding whom to evaluate for SAH and how to conduct this evaluation can be difficult. CT and LP are the mainstays of the emergency evaluation for SAH. Once the decision has been made to perform these tests, interpreting their results may also be challenging.[18] This article will review the current literature on the diagnosis and management of SAH. Emphasis will be placed on an algorithmic approach that is aimed at a rapid risk assessment utilizing history and physical examination and on the selective use and correct interpretation of CT and LP (Figure 1). Using this approach, patient outcomes may be optimized, while medicolegal risk may be reduced.

Etiology and Pathophysiology

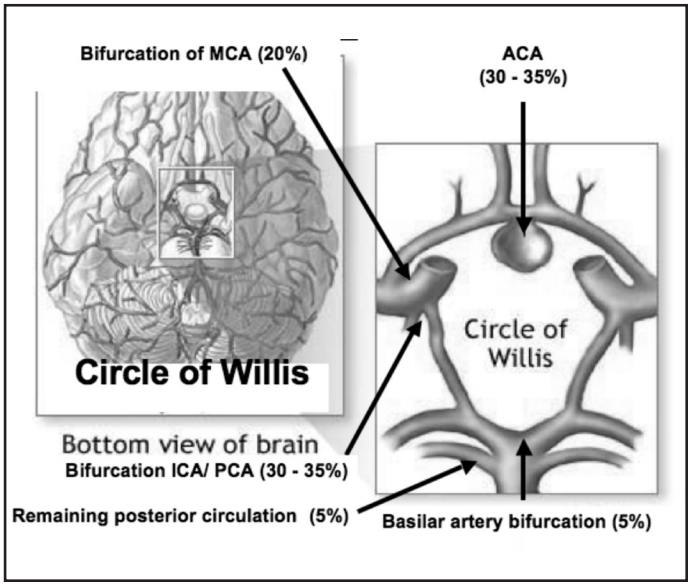
Subarachnoid hemorrhage occurs with an annual incidence of approximately eight people per 100,000 population per year.[19, 20] While most spontaneous cases of SAH are due to ruptured cerebral aneurysms, trauma remains the most common cause of SAH overall.[21,22] Eighty-five percent of spontaneous SAH result from rupture of saccular aneurysms arising in the vessels at the base of the brain. These vessels constitute the "Circle of Willis" (COW) (Figure 2A). Symmetrical to the sagittal plane, the circle of Willis is composed of anterior and posterior portions. The anterior portion is composed of the paired *anterior cerebral arteries*, joined by a single *anterior communication artery*, and the paired *internal carotid arteries*. Eighty-five percent of ruptured aneurysms arise from the anterior portion of the COW. Fifteen percent of ruptured aneurysms arise from the posterior portion of the COW, which is composed of the paired *posterior communicating arteries* and *paired posterior cerebral arteries* that originate at the bifurcation terminus of the basilar artery (Figure 2B). In contrast to a previous consensus that saccular intracranial aneurysms are always congenital, it is currently believed that aneurysms develop gradually over the lifetime of the patient. Such aneurysms occur in approximately 2% of asymptomatic adults.[22,23]

Figure 2A: Anatomy of the Circle of Willis



Several factors have been associated with a higher risk for aneurismal SAH (Table 1). These risks include a family history of intracranial aneurysms, connective tissue diseases, hypertension, smoking, atherosclerosis, oral contraceptives, older age, African-American and Japanese ethnicity, female sex, polycystic kidney disease, and heavy alcohol drinking.[24, 25] There is a three- to seven-fold increased risk of SAH in first-degree relatives of patients with SAH. African-Americans have a risk of 2.1:1, compared to Caucasians, while females are found to have a risk of 1.6:1, compared to men.[13]

Figure 2B: Location of aneurysms responsible for SAH



The risk of rupture increases as the size of the aneurysm increases. Aneurysms larger than 10 mm in diameter are five times more likely to rupture than are smaller ones. The annual risk of rupture for aneurysms <10 mm is 0.7%.[26]

Two scales that are widely used to grade the severity of SAH are the Hunt and Hess and the World Federation of Neurological Surgeons scales (Table 2).[27, 28] In both scales, there is a useful correlation between higher scores and worse patient outcomes. These scales should be used in conjunction with other clinical information to guide management. This information includes the size and location of the aneurysm and the overall condition of the patient.

Table 1: Risk Factors for Aneurysmal Subarachnoid Hemorrhage

- Family or personal history of SAH
- Smoking
- Alcohol abuse
- Cocaine, methamphetamine, MDMA use
- African American or Japanese ethnicity
- Hormone replacement therapy
- Diabetes mellitus
- Polycystic kidney disease
- Heritable connective tissue disorders
  - Ehlers-Danlos syndrome (Type IV)
  - Pseudoxanthoma elasticum
  - Fibromuscular dysplasia
- Sickle cell anemia
- Alpha1-antitrypsin deficiency

Table 2A: Hunt and Hess Severity Scale

Grade	Criteria
1	Asymptomatic, mild headache
2	Moderate to severe headache, nuchal rigidity, no focal deficit other than cranial nerve palsy
3	Mild mental status change (drowsy or confused), mild focal neurologic deficit
4	Stupor or moderate to severe hemiparesis
5	Comatose or decerebrate rigidity

Table 2B: World Federation of Neurological Surgeons

Grade	Glasgow Coma Scale	Focal neurological deficit
1	15	Absent
2	13-14	Absent
3	13-14	Present
4	7-12	Present or absent
5	3-6	Present or absent

History

Sudden onset and severe, or "thunderclap," headache has a broad differential diagnosis (Table 3). A rapid and organized clinical approach to these differential diagnoses is based upon a focused history and a directed physical examination. These are supplemented by selective laboratory testing when indicated. While approximately 10 to 15% of thunderclap headaches have been found to be associated with SAH, most SAH patients manifest the symptom of a sudden, severe headache.[1,29,30]

Approximately two-thirds of SAH present with isolated headache in the absence of neurological deficits. Three-quarters of SAH are associated with a "thunderclap" onset.[31] Specific historical features that may be useful in distinguishing SAH from other causes of headache are onset, severity, quality, and associated symptoms.[32] An abrupt onset of headache and a severity that is described as the "worst-ever headache" both suggest SAH. The headache is lateralized in 30% of patient, often ipsilateral to the side of the aneurysm. In one ED study, 12% of headache patients who responded, "Yes," to the question, "Is this the worst headache of your life?" or rated their headache pain a 10 on a 1-to-10 scale, had SAH.[6,13]

Table 3: Differential Diagnosis of Thunderclap Headache

- Subarachnoid hemorrhage
- Sentinel headache
- Cerebral venous thrombosis
- Cervical artery dissection
- Spontaneous intracranial hypotension
- Pituitary apoplexy
- Retroclival hematoma
- Ischemic stroke
- Acute hypertensive crisis
- Reversible cerebral vasoconstriction syndrome
- Colloid cyst of the third ventricle
- Acute complicated sinusitis
- Primary thunderclap headache
- Infections (e.g., acute complicated sinusitis)
- Acute myocardial infarction
- Anaplastic oligodendroglioma
- Aqueductal stenosis
- Pheochromocytoma
- Vogt-Koyanagi-Harada syndrome

If a headache presentation is described as unique or different in quality from other headaches, closer attention must also be paid. An adequate history will also determine if there are focal associated symptoms, such as neck stiffness syncope, double vision, or seizure. While seen in 75% of SAH, vomiting also occurs in up to half of benign causes of thunderclap headache. Thus, the presence of vomiting is poorly discriminatory. Seizures accompany SAH in 6% to 9%.[30] Fifty percent of patients presenting with SAH are found to have seizures, transient loss of consciousness, or altered level of consciousness.[30] Photophobia and visual changes may also be reported. Symptoms of meningeal irritation are present in more than three quarters of SAH, but may take several hours to develop. These include neck stiffness, low back pain, and bilateral neck pain. Historical features of SAH are summarized in Table 4.

In one prospective study of 102 emergency department patients with acute severe headaches suggestive of SAH only two characteristics, seizures and diplopia, were present only in patients with SAH.[30] These occurred so infrequently in SAH, however, that they were of little or no use for risk stratification.[30]

Physical Examination

The physical examination begins with an assessment of the vital signs and the airway, breathing, and circulatory status of the patient. Once stabilized, the patient is assessed by a focused neurological examination. This examination should search for the presence of mental status change, meningismus, cranial nerve palsies, nystagmus, leg weakness, abulia, anisocoria, ataxia, dizziness, hemiparesis, aphasia, neglect, Papilledema, and retinal hemorrhage. The proportion of patients with SAH who present with particular significant physical findings is summarized in Table 5.

Global or focal neurological abnormalities are found in more than 25% of patients, while no localizing signs are present in 40%. Neck stiffness is found in 60% of patients with SAH,

Table 4: Historical Features of SAH

Typical presentation
Sudden onset of severe headache, (frequently described as the "worst ever")
Nausea
Vomiting
Neck pain
Photophobia
Loss of consciousness
Atypical Features
Confusional state
Seizure
Associated head trauma

compared with 10% of benign thunderclap headaches in one small study.[31] One-quarter have motor deficits, abnormal speech, or inappropriate responses to commands.[33,34]

Certain physical findings in SAH may suggest the location of the aneurysm. Bilateral leg weakness and abulia are associated with anterior communicating artery lesions. Hemiparesis with aphasia or neglect are seen in middle cerebral artery aneurysms in 15% of cases. Nystagmus, ataxia, dizziness, and third nerve palsy are seen in posterior communicating aneurysms. Isolated third cranial nerve palsy is seen in some aneurysms near the junction of the internal carotid and posterior communicating arteries and is the most common cranial nerve palsy seen in SAH. Aneurismal neuropathy typically causes the pupil to be dilated because of compression of parasympathetic nerve fibers that run along the outside of the nerve. In contrast, third nerve dysfunction is most often due to infarction of the nerve from diabetes rather than aneurismal compression. In diabetic neuropathy there is flow from collateral vessels that results in sparing of the parasympathetic nerve fibers and, therefore, the pupil is reactive. Abducens nerve palsy and monocular vision loss may also be seen. Of note, the physical examination is entirely normal in many cases of SAH and thus is a nondiscriminatory finding.

Cerebrovascular Imaging

Noncontrast head CT is the initial laboratory examination to perform in patients with suspected SAH. CT has 90-98% sensitivity if performed within the first 24 hours of the bleed.[18] The sensitivity of CT for detecting SAH decreases with the time from the bleeding due to the reabsorption of blood within, and recirculation of, the CSF. In one review, sensitivity of CT on the day of aneurysm rupture was 92% and progressively decreased to 86%, 76%, and 58% on days 1, 2, and 5 post-rupture.[33-37]

Other limitations to CT include its use in patients with normal neurologic examinations and smaller volumes of hemorrhage who are less likely to have CT abnormalities. Anemia may also reduce the sensitivity of CT, and patients with hematocrit less than 30% may have bleeding that is not detectable because the blood is isodense with brain tissue.[38-43] Technical limitations of the scan, such as motion, bone artifacts, and inexpert interpretations, may also decrease its sensitivity.

Table 5: Physical Examination in SAH

Finding	Likely Location of Aneurysm
Mental status change • Seen in about one-fourth of patients[7,64,67]	Any
Meningismus • Seen in 60% of patients with subarachnoid hemorrhage[7] • Takes 3-12 hours to develop and may not be appreciated in comatose patients[68]	Any
Third nerve palsy[39,69] • 90% of patients with third nerve palsy due to aneurysm (versus other causes of third nerve palsy) have anisocoria>2mm[70]	Posterior communicating artery
Sixth nerve palsy[70,71] • Presents 3-14 days after onset of subarachnoid hemorrhage • Associated with higher clot burden • Gradually resolves	Any (due to increased intracranial pressure)
Bilateral leg weakness, abulia[15,35]	Anterior communicating artery
Nystagmus, ataxia, dizziness[15,35]	Posterior circulation
Hemiparesis with aphasia or neglect[15,35]	Middle cerebral artery
Subhyaloid (retinal) hemorrhage (Terson syndrome)[66] • Seen in about 10% of patients with subarachnoid hemorrhage • Associated with worse clinical grades on presentation and poorer prognosis	Any

The location of blood on a CT may suggest the etiology of the SAH. Blood from a ruptured aneurysm is usually located around the basal cisterns, while the blood is typically higher in the cerebral convexities in traumatic SAH.[32]

There is some debate in the current literature about whether a CT angiogram (CTA) may be used instead of a CT-then-LP workup sequence. This CTA-only approach to sudden severe headache is partly a response to the evidence that fewer than half of these patients, when the initial CT is negative, then undergo LP in actual practice.[40,41,44]

In one well-designed prospective study of CTA in 116 patients, six cases of aneurysms were detected that had not been seen on noncontrast CT.[45] All of these patients had a positive LP result; but there were also three cases of negative CT and negative spinal fluid that had a positive CTA. These cases were thought to represent unruptured aneurysms. Since approximately 2% of the general population harbors intracranial aneurysms, a CTA-first approach might subject headache patients to unnecessary risks of angiography, interventional radiology, and surgery. Some patients have iodine dye allergies or renal insufficiency, further limiting the utility of CTA as a primary diagnostic tool in suspected SAH.[32]

The role of magnetic resonance imaging (MRI) in the evaluation of SAH has also been studied. MRI is superior to CT in detecting subacute and chronic SAH, especially with fluid-attenuated inversion recovery (FLAIR) and T2-weighted imaging.[45-50] FLAIR sequence MRI negates the signal from CSF, permitting the detection of tiny amounts of blood in the subarachnoid space. A small 2004 study identified 12 cases of acute SAH in which CT was negative for SAH and LP was positive for SAH. FLAIR MRI findings were positive in only two of these cases and were false negative in ten.[57] Because of this and because MRI is of limited availability in most EDs, MRI is not currently recommended to replace LP in the evaluation of SAH.[51-58]

Considerable literature exists regarding the optimal imaging modality for the planning of definitive therapy of SAH.[57,58,62-66] The choice of the modality for cerebrovascular imaging to be used to identify the aneurysm will depend in large part upon the preference of the neurosurgical consultant.[55-61,67-69] Cerebral digital subtraction angiography (DSA) has for many years been considered the imaging technique of choice for preoperative imaging of SAH. DSA identifies the bleeding site, size, and location of the aneurysm, and it maps the relevant operative anatomy and elucidates vascular anatomy.[69] Angiography may be negative in 10% to 20% of patients with SAH because of perimesencephalic hemorrhage, vasospasm, thrombosed aneurysm, or other rare causes.[47]

Cerebral computed tomographic angiography (CTA) is rapidly replacing DSA as the primary neurosurgical planning study. Its sensitivity and specificity are comparable to DSA, and it is widely available, fast, and noninvasive.[48]

MRA is another imaging study that, while widely available for the diagnosis and neurosurgical planning for SAH, is less well studied.[47,50,57,59,70] The choice of imaging modality for neurosurgical planning is best made in consultation with the neurosurgeon or neuroradiological interventionalist. In many cases definitive treatment of SAH is now being accomplished by endovascular techniques at the same time as the initial diagnostic angiogram. Because of the sequential dye loads entailed during these two phases of diagnosis and treatment, thoughtful coordination of these steps by the neurosurgeon and neuroradiologist are especially important.

Role of Lumbar Puncture

Because of the limitations of CT as outlined above, all patients with suspected SAH who have a negative CT should undergo lumbar puncture.[39] This is especially important in awake, neurologically intact patients who present with sudden, severe headaches. Such patients are particularly likely to have a negative CT despite the presence of SAH. In one study, only 25-50% of such patients underwent LP after a normal CT.[40] In another study, 10% of neurologically normal ED patients with acute headache were diagnosed on the basis of positive CSF results after a normal cranial CT.[41] Other studies have determined that 2-7% of CT negative SAH patients were ultimately picked up by positive LP results.[13, 36, 42, 43]

The cerebrospinal fluid (CSF) obtained by LP should be assessed for the presence of red blood cells (RBCs) and for xanthochromia. An absolute number of RBCs that establishes the diagnosis of SAH has never been established.[32] A traumatic tap is estimated to occur in 10-15% of LPs.[44] Typically, progressive clearing of blood in each succeeding tube of CSF of the four collected represents evidence that the tap was traumatic. Ideally, if the final tube has zero RBCs, it may be concluded with confidence that the tap was traumatic. When a less than complete clearing of RBCs is demonstrated, the higher the RBC count in the final tube, the more likely it is that a true positive (i.e., SAH) is present. In this situation, additional diagnostic testing may be indicated and includes computed tomographic angiography (CTA), magnetic resonance angiography (MRA), or conventional cerebral angiography.[45-50]

Xanthochromia refers to a yellow discoloration that may be detected in CSF that suggests the presence of SAH. This discoloration results from the enzymatic breakdown of red blood cells in the CSF, and it is rarely seen within the first four hours of SAH. Xanthochromia usually requires at least six hours, and sometimes up to 12 hours, to develop after SAH. Xanthochromia is detected either by spectrophotometry or by simple visual comparison of the CSF sample to an equal volume of water against a white background. Although spectrophotometry, more commonly employed in Europe, is the most sensitive method of detection of xanthochromia, many hospital laboratories in the United States rely upon simple visual inspection of the CSF sample. The absence of xanthochromia by either visual or spectrophotometric analysis has a high negative predictive value for SAH, with one estimate of 99%.[51] Several

conditions may create false positive xanthochromia, including jaundice (total bilirubin > 0-15 mg/dL), increased cerebrospinal fluid protein (>150 mg/dL), rifampin use, and excess dietary carotenoids.[32] Xanthochromia may persist for up to two weeks following SAH.[52]

Measurement of the opening pressure (OP) is also useful in the evaluation for SAH. OP is elevated to >20 cm H_20 in 60% of patients with SAH.[52] CSF pressures may also be elevated in cerebral venous thrombosis and in idiopathic intracranial hypertension, and low pressures may be seen in spontaneous intracranial hypotension.[53,54]

Initial Management

Once the diagnosis of SAH is confirmed, the priorities are: 1) airway management, 2) analgesics, 3) arrhythmia monitoring, 4) blood pressure control, 5) seizure prophylaxis, 6) vasospasm prophylaxis, 7) hydration, and 8) hydrocephalus management.

Simultaneously, an immediate call should be made to a neurosurgeon. In this way, further imaging and management of the patient may be coordinated while definitive care is arranged. Next, some form of cerebrovascular imaging is obtained in consultation with neurosurgery (e.g., magnetic resonance angiography [MRA], CT angiogram [CTA], or traditional cerebral angiography- see "Cerebrovascular Imaging," above).

Airway Management

Airway management is chosen based upon usual clinical criteria. Endotracheal intubation is almost never needed in patients with mild SAH (grades 1-3), while for more severely affected patients (grades 4 and 5 or Glasgow Coma Scale of ≤8), most will require intubation for airway protection, oxygenation and/or ventilation. Rapid sequence intubation should be used. While the efficacy of lidocaine and/or fentanyl to blunt the rise in intracranial pressure in this setting is unclear, it is the author's practice to use them. Short-acting agents with attention to adequate sedation should be used for rapid-sequence protocols, so that the neurological examination can be followed by the consulting neurosurgeon. In most circumstances, a quick baseline neurological examination prior to drug administration should be performed and documented. Thiopental and etomidate are optimal induction agents in SAH; the former has a cytoprotective effect, but its use is limited to hypertensive patients because of its tendency to drop systolic BP. Hyper- and hypoventilation are to be avoided, with a target pCO_2 of 30-35 mmHg.

A rapid baseline neurological examination should be performed and documented prior to drug administration, and subsequent excessive sedation is minimized so as to allow serial neurological examinations. Excessive sedation has also been reported to increase ICP directly.[55]

The patient is placed at bed rest with the head of the bed elevated 30° and is given nothing by mouth except for medications.

Analgesia

Analgesia is provided for severe headache and for painful procedures, using small doses of a short-acting, reversible agent. Sedation is provided to intubated patients, preferably with short-acting, titratable or reversible medications that allow repeat neurological examinations.

Arrhythmia Monitoring

Subarachnoid hemorrhage is associated with symptomatic bradycardia, ventricular tachycardia, and ventricular fibrillation. A variety of twelve-lead electrocardiogram changes have also been described, including ST-segment elevation or depression, QT interval prolongation, and T-wave abnormalities, often mimicking myocardial ischemia or infarction.[55, 58]

In their 2009 guidelines on management of SAH, the American Heart Association has recommended that all patients with SAH be treated in an intensive care unit setting with cardiac and blood pressure monitoring.[57]

Blood pressure is managed, aiming at a target blood pressure goal chosen in consultation with the neurosurgical critical care team. The available research on the control of blood pressure in SAH is inconclusive and contradictory, and individual practices vary.[21,34,39,55, 62,63,64] Control of blood pressure reduces the rate of rebleeding, but this reduction is achieved at the expense of increasing the rate of cerebral infarction; the rate of rebleeding was 15% in patients treated with antihypertensives, compared with 33% in the nontreated group. But the rate of cerebral infarction doubled in the treatment group compared with the nontreatment group (40% vs. 22%).[60,61] Most centers begin to address blood pressure by treating pain, anxiety, and nausea. Stool softeners are also commonly administered.[58]

There is no consensus on the degree to which blood pressure should be reduced. Suarez et al. have recommended that systolic blood pressure (SBP) be maintained at 90-140 mm Hg before aneurysm treatment, after which SBP of ≤ 200 mm Hg is permitted.[21] If blood pressure reduction is chosen, this is often accomplished with short-acting intravenous agents, such as labetalol, nicardipine, and esmolol.[32,39,62-64] Nitroprusside and nitroglycerine are generally avoided because of their potential to increase intracranial pressure (ICP).[58] Vasopressor agents and optimal preload; i.e., central venous pressure (CVP) 5-8 mm Hg, may be required to maintain SBP over 120 mm Hg in order to avoid further CNS damage in the ischemic penumbra due to vasospasm that is seen in SAH (see section below on vasospasm management). In the event of vasospasm, a higher CVP of 8-12 mm Hg, or a pulmonary capillary wedge pressure (PCWP) of 12-12 mm Hg, is recommended.[21]

Seizure Prophylaxis

Antiepileptic drugs (AEDs) are widely administered to prevent seizures in patients with SAH, but their use continues to be a subject of debate.[58] A loading dose of phenytoin, or its equivalent, is often given early in the course of ICU stabilization.

Barbiturates or benzodiazepines are avoided as first-line AEDs, because they tend to over-sedate the patient, masking potentially neurologic examination findings.[55] While the prevention of seizure activity and resulting secondary brain injury is reasonable, one large series has found that AED exposure may be correlated with worse cognitive and neurologic outcome.[62] In the setting of perimesencephalic blood without cortical layering; i.e., blood only at the base of the brain, conferring a good prognosis, withholding of AEDs seems to be reasonable. After definitive treatment of the aneurysm in patients without acute seizures and with a lower grade SAH, discontinuation of AED is often recommended.[58, 59]

Vasospasm Prophylaxis

Vasospasm occurs in up to 30% of patients with SAH, and it is the leading cause of death and disability after aneurysm rupture.[33, 59] It is manifested by a decline in neurological status, usually occurring after 72 hours from the ictus, and peaking at the eighth day. Vasospasm may develop up to two weeks after SAH, and it carries significant risk of morbidity from cerebral infarction.[21,32,34,39,43,62-67] Some authors have recommended that transcranial Doppler (TCD) ultrasonography measurement be taken at baseline and during treatment to monitor for vasospasm.[58]

Nimodipine is a calcium channel blocker that is given orally or by nasogastric route, at a dose of 60 mg every four hours. Nimodipine treatment reduces poor outcomes, though the mechanism remains unclear.[61,65] It has been noted that, contrary to popular belief, nimodipine does not prevent or treat the vasospasm itself. While nimodipine is initiated as soon as possible after SAH, aggressive therapy for vasospasm itself is only appropriate after occlusive therapy of the aneurysm.[58] Intraluminal papavarine and angioplasty have both been employed to treat vasospasm. Other means of treating vasospam include hemodilution, induced hypertension, and hypervolemia (also known as "triple-H therapy').[58]

Hydration

The hydration status of the patient has been referred to above in the section on Blood Pressure Management. Treatment of hypotension with a goal of optimizing cerebral perfusion pressure requires appropriate invasive monitoring; e.g., swan-ganz, ventriculostomy, central venous pressure monitor, arterial pressure monitor. A CVP of 5-8 mm Hg may be required to maintain SBP over 120 mm Hg. in order to avoid further CNS damage in SAH. In the event of vasospasm, a higher CVP of 8-12 mm Hg or a pulmonary capillary wedge pressure (PCWP) of 12-12 mm Hg is recommended.[21]

Table 6: SAH Practice Guidelines

A. 2008 American College Of Emergency Physicians Clinical Policy On Acute Headache (Evidence-Based Recommendations)[19]

1. Emergent head computed tomography **IS** the initial diagnostic test recommended in the diagnosis of any new, sudden-onset, severe headache or suspected case of subarachnoid hemorrhage* (*Class I, Level B recommendation*).[20-26]
2. Lumbar puncture **IS** recommended for patients with suspected subarachnoid hemorrhage after negative noncontrast head computed tomography* (*Class I, Level B recommendation*).[20-22]
3. Angiography is **NOT** recommended in patients with sudden-onset, severe headache who have negative findings on head computed tomography, normal opening pressure, and negative cerebrospinal fluid findings (*Class II, Level B recommendation*).
4. Patients with a negative workup including negative computed tomography and lumbar puncture **CAN** be safely discharged from the emergency department, with outpatient follow-up recommended (*Class II, Level B recommendation*).
5. Response to analgesia should **NOT** be used as the sole indicator to the etiology of an acute headache (*Class III, Level C recommendation*).

**Also supported by 2009 American Heart Association guidelines.*

B. 2009 American Heart Association Guidelines For Management Of Subarachnoid Hemorrhage (Evidence-Based Recommendations)[20]

Recommendations for diagnostic studies

1. Once subarachnoid hemorrhage is diagnosed, urgent cerebral angiography **IS** needed to detect the underlying cerebral aneurysm (*Class I, Level B recommendation*).[20,21]
2. When conventional angiography cannot be performed in a timely fashion, magnetic resonance angiography and computed tomographic angiography **MAY** be considered (*Class III, Level B recommendation*).[20]

Recommendations for management

1. Patients with subarachnoid hemorrhage should be treated in an intensive care unit setting with cardiac and blood pressure monitoring (*Class I, Level B recommendation*).[20,21,25]
2. Control of elevated blood pressure **IS** recommended to balance the risk of stroke, rebleeding, and maintenance of cerebral perfusion pressure (*Class II, Level B recommendation*).[20,25]
3. Oral nimodipine **IS** strongly recommended to reduce poor outcome from vasospasm (*Class I, Level A recommendation*).[20,21]
4. Prophylactic anticonvulsant therapy **MAY** be considered in the immediate posthemorrhage period (*Class III, Level B recommendation*).[20,21,25]
5. Early surgery **IS** recommended for most patients (*Class II, Level B recommendation*).[20,21]

Recommendations for transfer

1. Early referral to high-volume centers with cerebrovascular surgeons and endovascular services **IS** recommended (*Class II, Level B recommendation*).[20,21,27]

In contrast, overhydration of the patient is avoided as this increases the risk of hydrocephalus, which is discussed below.

Hydrocephalus

Hydrocephalus may develop within the first 24 hours of the SAH, either as a result of clotted blood products obstructing the flow of CSF or by decreased absorption of CSF at the arachnoid granulations.[64] In one study, hydrocephalus was documented in 15% of patients by CT scan, of whom almost one-half were asymptomatic.[64] Factors correlated with the development of hydrocephalus include intraventricular hemorrhage, treatment with antifibrinolytic agents, posterior circulation SAH, low GCS on presentation, history of hypertension in patients with hyponatremia. One-half of patients with acute hydrocephalus and decreased level of consciousness will spontaneously improve, while the other half experience rebleeding, infarction, and increased morbidity and mortality.

Ventricular drain placement is considered for patients with hydrocephalus and decreasing level of consciousness and for those whose hydrocephalus does not improve within 24 hours.[65]

Reversal of Anticoagulation

The American Heart Association/American Stroke Association guidelines recommend discontinuation of all antiplatelet and anticoagulant medications after SAH. In addition, immediate reversal of any anticoagulant effect is advised for SAH until definitive surgery or coiling of the aneurysm.[32,66,67] Intravenous vitamin K and fresh frozen plasma (FFP) or prothrombin complex concentrates (PCC) may be required. PCC has been associated with a faster reversal in international normalized ratio (INR) when compared to FFP.[32,34,68] The use of recombinant human factor VIIa has also been described.[57,69] Management of a supratherapeutic International Normalized Ratio (INR) has been published.[57,69] Specifically, warfarin is withheld and 10 mg vitamin K1 is administered by slow IV infusion. Anaphylactoid reactions to intravenous vitamin K have been documented in a small number of cases despite the widespread use of this drug. This suggests that the reaction is rare. Additionally, anaphylactic reactions and case fatality reports may occur even when intravenous vitamin K is given at low doses by slow dilute infusion.[69-73]

Intravenous vitamin K_1 should be diluted and given at a slow rate (less than 1 mg/min) because of the danger of systemic reactions, including hypotension.[71] Avoidance of hypotension is of paramount importance in SAH in order to maintain CPP.

Definitive Management

Definitive management of SAH from aneurysm rupture involves either surgical clipping or endovascular ablation. In contrast to earlier protocols, definitive repair now usually takes place within 72 hours of the bleed.[13,27,32,34,38,39,43,55,58,60,61,63,72,73,83]

Improved outcomes have been achieved for eligible patients who underwent endovascular coiling, in comparison to surgical clipping.[74] Each patient is best evaluated individually for clipping versus coiling, based on anatomical characteristics of the aneurysm, the experience of the treating physicians as well as on the patient's clinical status.[74,75]

Whether they are treated by surgical clipping or by endovascular coiling, patients with SAH have better outcomes when treated in high-volume centers.[32,76-80]

Whenever feasible, SAH patients should be transferred to such specialized neuroscience centers, and such transfer has been found in one prospective study to be both safe and expeditious. In that study, the average time to effect transfer (measured from time of SAH diagnosis to arrival at the receiving facility) was five hours. Only 10% of these patients had a significant decrease in Glasgow coma scale (GCS). Prearranged transfer agreements between community hospitals and referral centers are likely to facilitate and expedite such transfers.[77]

Complications

Complications occurring after SAH include rebleeding, vasospasm, hydrocephalus, hypothalamic dysfunction, hyponatremia, aspiration pneumonia, and left ventricular (LV) systolic dysfunction. The subjects of vasospasm and hydrocephalus and their treatment have been addressed previously (see Initial Stabilization and Management).

Rebleeding occurs in approximately 15%-20% of patients within the first few hours of SAH.[32,55,58,61,68-82] Rebleeding carries a mortality risk of 40% without intervention.[21]

If the diagnosis of SAH is missed initially, those patients who present in good clinical condition are five times more likely to rebleed and nine times more likely to have poor outcomes than those who are diagnosed without delay.[15,18,55,58] Rebleeding appears to occur with greater frequency in patients with higher Hunt and Hess scores. Control of blood pressure and antifibrinolytic therapies were the principle means of minimizing rebleeding rates in an earlier era in which definitive repair was delayed for weeks after the SAH. Current concepts empha-

Table 7: Complications of SAH

Complications
Hydrocephalus
Rebleeding of subarachnoid hemorrhage
Vasospasm
Neurologic deficits
Hypothalamic dysfunction which may lead to - Myocardial ischemia or - Labile detrimental BP.
Hyponatremia
Aspiration pneumonia and other complications of critical care.
Left ventricular systolic dysfunction

size early definitive care as the ideal way to prevent rebleeding, which increases when definitive aneurysm repair is delayed.[57,58]

Hypothalamic dysfunction after SAH may result in excessive sympathetic stimulation, which in turn may cause labile and detrimental blood pressure fluxes and myocardial ischemia.

Aspiration pneumonia, deep venous thrombosis (DVT), and the full range of other typical ICU complications are also seen after SAH. Airway protection is achieved by ETT or by keeping the patient NPO until a formal swallowing evaluation is performed. Nasogastric intubation or percutaneous gastrostomy tubes may be required for enteral nutrition of the SAH patient who fails a swallowing study.

DVT prophylaxis with subcutaneous heparin and serial compression devices are considered or given at the time of SAH. One author has recommended that pneumatic compression stockings be applied prior to aneurysm treatment and that subcutaneous unfractionated heparin 5,000 units three times a day be added once the aneurysm is treated.[65] A Joint Commission performance measure is that DVT prophylaxis be initiated by 48 hours after SAH.

Hyponatremia in SAH results either from inappropriate secretion of antidiuretic hormone (SIADH) characterized by normal or increased intravascular volume or, less commonly, from cerebral salt wasting, with low intravascular volume.[83,84] Treatment of hyponatremia due to SIADH typically consists of fluid restriction, but this may not be appropriate for patients with SAH because it may promote cerebral vasospasm. Instead, hyponatremic patients with SAH should be treated with hypertonic (3%) saline in order to support cerebral perfusion and to prevent hyponatremia-induced brain swelling. Fluid administration is indicated for cerebral salt wasting. Patients with SAH should be kept euvolemic, since hypovolemia is associated with cerebral ischemia and a worse outcome.[85-88]

Cardiac abnormalities associated with SAH include cardiac biomarkers elevation, electrocardiographic changes, and left ventricular (LV) systolic dysfunction. The mechanisms of cardiac dysfunction after SAH remain controversial. In one study regional wall motion abnormalities were present in 35% of patients with Hunt & Hess grades 3 – 5.[88] Up to 20% of patients with SAH demonstrate elevated troponin I levels, and these patients are more likely to have EKG abnormalities and clinical evidence of left ventricular dysfunction. EKG abnormalities include ST segment depression, QT interval prolongation, deep T wave inversions, and U waves. Life-threatening dysrrhythmias, including torsades de pointes, have been reported as well as atrial fibrillation and flutter.[58]

Discussion

Role of the "Warning" Headache

A "sentinel" or "warning" headache is a sudden, severe headache that resolves and that is retrospectively identified to have occurred days to weeks before the SAH. Sentinel bleeds, only diagnosed in retrospect, are believed to occur in 10% to 40% of SAH patients.[1-3,9-13,15,23, 32,34,60,61,81,82] The reasons that have been suggested to explain the phenomenon of the sentinel headache include recall bias, initial misdiagnosis of SAH, and minor initial leak of an aneurysm. It has been noted that patients with a sentinel bleed have higher rates of rebleeding and a higher mortality than those without one.[61]

LP-First Strategy

Although the general recommendation is that CT, followed by LP, is the appropriate diagnostic sequence in the majority of patients with suspected SAH, there are proponents of performing the LP first in selected patients.[6-16,29,32,35,41,46,82,83] Advocates of this strategy reason that certain patients who are neurologically normal and without evidence of increased ICP could undergo an LP alone, which, if normal, would allow for safe discharge from the ED. In this way some patients could be spared the time, expense, and radiation exposure of CT. Critics of this approach argue that the removal of CSF from patients with unrecognized intracranial hematomas may precipitate herniation and rebleeding, each of which carries a significant morbidity.[55,56] These critics also cite the fact that CT may identify other causes of sudden, severe headache, such as paranasal sinusitis and venous sinus thrombosis. No prospective studies are yet available on the effectiveness of the LP-first approach. In one recent retrospective study, 5% of patients with spontaneous SAH and normal neurological exams had computed tomographic findings that contraindicated lumbar puncture.[89]

For these reasons CT followed by LP remains the standard current recommendation for the diagnostic testing in suspected SAH.[43,51]

CT Scanning Alone (Without LP)

CT imaging could be used as a definitive diagnostic study in SAH patients if its diagnostic sensitivity was sufficiently high. Some authors have suggested that fifth generation CT scanners possess this sensitivity. In one recent study from Denmark**,** 296 patients were found to have a SAH.[90] In 295 of these patients the diagnosis was based on a positive CT scan. In a single patient, on day six after SAH, the diagnosis was based on a positive lumbar puncture. From day one to day five in this study, CT scanning was found to have a sensitivity of 100%. Overall, CT scanning had a sensitivity of 99.7 %. CT scanning was demonstrated to be excellent as a lone diagnostic test in the first days after ictus and a negative CT scan was sufficient to exclude SAH. These authors suggested omitting LP in the first three days after ictus, if the results of the CT scan are negative. Similarly, in a paper by Boesinger et al. patients presented with headache and had a CT scan of the head with a fifth generation multi-detector CT scanner followed by a LP to rule out SAH. There were 177 patients who presented to the ED with headache and who went on to have a CT scan and an LP to rule out SAH. No patients who had a negative CT were found to have a SAH. It was concluded that fifth generation CT scanners are probably more sensitive than earlier scanners at detecting SAH.[91]

In contrast, Byyny et al. evaluated the sensitivity of noncontrast cranial CT in detecting all spontaneous subarachnoid hemorrhages and found an insufficient sensitivity as a stand-alone test.[42] This was a retrospective review that identified 149 patients with SAH in whom noncontrast cranial CT scan diagnosed SAH in 139 patients. The remaining ten patients had SAH diagnosed by LP. Thus, CT scan sensitivity was only 93%. For the 67 patients presenting with headache and normal mental status that had a SAH and vascular lesions (either aneurysm or arteriovenous malformation), the sensitivity of cranial CT scan was 91%. The authors concluded that noncontrast CT imaging exhibited inadequate sensitivity to serve as a sole diagnostic modality in detecting SAH. The ACEP clinical policy on the management of patients presenting to the emergency department with headache states that, "In patients presenting to the ED with sudden-onset, severe headache and a negative noncontrast head CT scan result, lumbar puncture should be performed to rule out subarachnoid hemorrhage." [42,43]

Early deterioration in the SAH patient's neurological status may occur due to cerebral infarction, rebleeding, hydrocephalus, or subdural extension. Repeating the CT scan in cases of acute decline in neurological status is recommended because some of these etiologies are potentially reversible.[32, 43, 62, 64, 85]

Prognosis

Ten to 15% of patients with SAH die before reaching medical care. In-hospital mortality for SAH is approximately 30%. Thirty-day mortality of SAH approaches 50%.[15,18,21,23,32,34,43,62,78]

The occurrence of rebleeding after SAH is the single most prognostic factor, conferring an 80% rate of mortality or serious disability. Other significant prognostic factors are age, comorbity, perioperative complications, vasospasm, level of consciousness and clinical grade of bleeding at time of presentation, and amount of blood on initial head CT. Other conditions associated with poor prognosisis are hyperglycemia, fever (both infectious and non-infectious), cerebral infarction and symptomatic vasospasm, and renal insufficiency.[58] Long-term disability occurs in up to half of all SAH patients and includes cognitive and other neurological deficits and epilepsy.[32]

Summary

Of the approximately 120 million patients who present to America's emergency departments annually, over two million will have a chief complaint of headache. Approximately 2% of these patients, or 27,000, have SAH. Of these, almost one-half, or 14,000, will die within the first month after hemorrhage. Of the 14,000 patients who survive more than a month, over half will have a serious and permanent neurological disability, especially when the diagnosis is delayed.

When faced with a patient with a sudden-onset, severe headache, the physician must do the following rapidly: 1) conduct an expeditious history and physical examination, 2) perform an emergent non-contrast CT scan, and 3) if it is negative, perform an LP. At the same time, the clinician must be aware of the limitations of these studies, and must be expert in their interpretation. Because of the wide spectrum of complaints in, and the atypical presentations of, patients with SAH, missed diagnoses occur with alarming frequency.[5,7,9-13,15,16,18,21,23,29-32,34,37,43,55-57,8]

Emergency physicians must stabilize the SAH patient, beginning with basic cardiorespiratory monitoring and resuscitation, and then by reversal of anticoagulation and by neurologic management, including nimodipine, to improve outcomes related to vasopasm, and optimization of cerebral perfusion. If SAH is diagnosed, prompt and appropriate cerebrovascular imaging will be needed. It should be ordered in consultation with the receiving neurosurgeon or interventional neuroradiologist.[91]

Finally, because patients with SAH fare better when they are transferred to high volume neurocritical care centers, such transfer should be arranged if possible. Once there, neurosurgical clipping or endovascular coiling of the aneurysms may be accomplished.

David M. Lemonick, MD, FAAEP, FACEP, is Attending Physician, Emergency Department, Armstrong County Medical Center in Kittanning, PA. Originally residency-trained in general and cardiothoracic surgery, Dr. Lemonick has practiced emergency medicine for more than 20 years.

Potential Financial Conflicts of Interest: By AJCM® policy, all authors are required to disclose any and all commercial, financial, and other relationships in any way related to the subject of this article that might create any potential conflict of interest. The author has stated that no such relationships exist.

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