TABLE 165-8 Metabolic Causes of Headache

History	Examples	Treatment
Hypoxia/hypercapnia	High altitude	Acetaminophen/ibuprofen Acetazolamide 125–250 milligrams twice a day Steroids (dexamethasone) Prophylaxis: acetylsalicylic acid, 320 milligrams at 4-h intervals, starting 1 h prior to ascent; repeat 3 times
	Air travel	Nonsteroidal anti-inflammatory drugs (NSAIDs), pseudoephedrine, and nasal decongestants
	Pulmonary disease Congestive heart failure Sleep apnea	
Dialysis		NSAIDs/analgesics during dialysis
Autonomic dysreflexia (typical in quadriplegia)		Seated position Remove/loosen clothing Scrutinize for bladder distension/bowel impaction
Other	Hypothyroidism Fasting Cardiac cephalgia (associated with myocardial ischemia)	

The headache location tends to be retro-orbital, bifrontal, or suboccipital. Between 63% and 100% of patients will experience headache.[81] Associated symptoms may include ophthalmoplegia, reduced visual acuity, visual field defects, altered consciousness, meningismus, and nausea and vomiting. CT (noncontrast) and MRI may show a sellar mass and hemorrhage. In the first 1 to 2 hours, the hyperacute hemorrhage may be easier to see on CT than MRI. Pituitary adenomas and cerebral aneurysms have a co-occurrence rate of 7.4%.[81] Pituitary tumor apoplexy requires immediate treatment with corticosteroids and urgent neurosurgical consultation. The treatment usually requires consultations from endocrinology, ophthalmology, and neurology with intensive care monitoring.

THIRD VENTRICLE COLLOID CYSTS

Colloid cysts of the third ventricle are a rare cause of acute neurologic deterioration and sudden death. The colloid cyst is usually congenital, slow growing, and benign, accounting for about 0.2% to 2% of all intracranial tumors, but it is the most common tumor of the third ventricle.[82] The usual clinical presentation is a history of severe paroxysmal and episodic attacks of (typically frontal) headache associated with nausea and vomiting. The presumptive cause is the intermittent obstruction of cerebrospinal fluid flow through the foramina of Monro with associated rapid increase in intracranial pressure.[83]

SINUSITIS

Classic features of purulent nasal discharge, nasal or facial congestion, hyposomia, or anosmia with or without fever, along with headache, ear pain or fullness, halitosis, and dental pain, allow for clinical diagnosis of **sinusitis**,[84] and treatment with antibiotics is warranted.

REFERENCES

The complete reference list is available online at www.TintinalliEM.com.

CHAPTER 166

Spontaneous Subarachnoid and Intracerebral Hemorrhage

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O. John Ma

INTRODUCTION

Although nontraumatic subarachnoid and intracerebral hemorrhages account for a relatively small portion of ED visits, a missed diagnosis can produce devastating results. Early recognition and aggressive management may improve outcomes.

Subarachnoid hemorrhage is the leakage of blood into the subarachnoid space, most often due to a ruptured intracranial aneurysm. The classic presentation is a sudden, severe headache.

Intracerebral hemorrhage, or hemorrhagic stroke, typically presents as an acute neurologic deficit, often accompanied by headache. The features and treatment of subarachnoid and intracerebral hemorrhage are discussed in this chapter. Management of intracerebral hemorrhage is very different from the management of ischemic stroke. Ischemic stroke is discussed in chapter 167, Stroke Syndromes.

SUBARACHNOID HEMORRHAGE

EPIDEMIOLOGY

About 75% of subarachnoid hemorrhages are caused by a ruptured aneurysm. In about 20%, a cause is not identified.[1] The remaining causes are related to a variety of miscellaneous conditions, including arteriovenous malformations, sympathomimetic drugs, and other less common causes. About 20% of patients with one aneurysm will have an additional aneurysm, which makes identification of the initial aneurysm important.

Two percent of family members of patients with subarachnoid hemorrhage will develop the same disease. This risk rises with increasing number of family members involved or with a family history of adult polycystic kidney disease.[1] Hypertension and smoking increase the risk. Additional risk factors are listed in **Table 166-1**.

PATHOPHYSIOLOGY

Cerebral aneurysms are focal arterial pouches typically located in areas of bifurcation of the circle of Willis. While the precise pathophysiology is not known, many factors have been associated with aneurysmal development and rupture. Such factors include familial/genetic predisposition, cellular aberrations in vascular wall repair or remodeling, and aberrations in local blood flow.[2] While it is not possible to predict rupture risk of a particular aneurysm, larger aneurysms (>5–10 mm) are more likely to rupture than smaller aneurysms.[2,3]

TABLE 166-1 Risk Factors for Subarachnoid Hemorrhage

Hypertension
Smoking
Excessive alcohol consumption
Polycystic kidney disease
Family history of subarachnoid hemorrhage
Coarctation of the aorta
Marfan's syndrome
Ehlers-Danlos syndrome type IV
α_1-Antitrypsin deficiency

CLINICAL FEATURES

Patients with subarachnoid hemorrhage classically present to the ED with a severe headache of acute onset (termed a "thunderclap" headache) that reaches maximal intensity within minutes. Typically, the headache persists for several days, but may resolve in a shorter period.[1] Subarachnoid hemorrhage is diagnosed in 11% to 25% of patients who present to the ED with a thunderclap headache.[4,5] **Even if a patient is not experiencing the "worst ever" headache, a headache that is different in intensity or quality from past headaches raises concern for subarachnoid hemorrhage.** Headaches associated with loss of consciousness, seizure, diplopia or other neurologic signs, or nuchal rigidity also require clinical investigation.[6] Less frequently, patients may present with nausea and vomiting, altered mental status, photophobia, or symptoms suggestive of ischemic stroke. Approximately 20% of patients develop their symptoms while engaged in activities that cause increased blood pressure, such as exercise, sexual intercourse, or defecation. Isolated, uncomplicated true syncope without head trauma, headache, seizure, neurologic deficits, nuchal rigidity, or other symptoms of subarachnoid hemorrhage does not require evaluation for subarachnoid hemorrhage. In the absence of blunt trauma, subhyaloid retinal hemorrhage is pathognomonic of subarachnoid hemorrhage but is not commonly seen.

DIAGNOSIS

Patients with subarachnoid hemorrhage who are misdiagnosed at their initial ED visit have worse outcomes than those who are diagnosed early.[7,8] Misdiagnosis is associated with normal mental status (present in about half of patients with subarachnoid hemorrhage) and smaller size of hemorrhage.[8] Complications of missed diagnosis include repeat hemorrhage and obstructive hydrocephalus. Symptomatic improvement following analgesics does not exclude life-threatening causes of headache.[9] **Table 166-2** lists the differential diagnosis of subarachnoid hemorrhage.

Imaging The initial diagnostic modality of choice when subarachnoid hemorrhage is suspected is a noncontrast CT of the head (**Figures 166-1** and **166-2**). **The sensitivity of CT in diagnosing subarachnoid hemorrhage is highest shortly after symptoms begin and is estimated to be 98% within 6 to 12 hours of the onset of symptoms.** Sensitivity decreases to about 91% to 93% at 24 hours and continues to decline rapidly thereafter, reaching 50% at 1 week.[6,9] Newer-generation CT scanners provide increased sensitivity for detecting subarachnoid hemorrhage, especially in the setting of (1) patients presenting within 6 hours of symptom onset, and (2) greater availability of a timely interpretation by a neuroradiologist.[10-12] For suspected subarachnoid hemorrhage, a negative head CT is typically followed by LP (see later discussion).

CT/CT angiography (CTA) and MRI/MRA are options after a negative head CT, when these studies are clinically appropriate and available.[13] In a small study, two of 116 patients had an aneurysm discovered by CTA after normal findings on both CT and LP.[14] The probability of excluding a subarachnoid hemorrhage following CT/CTA is about 99.4%.[15]

TABLE 166-2 Differential Diagnosis of Subarachnoid Hemorrhage

Vascular (other intracranial hemorrhage, ischemic stroke or transient ischemic attack, arterial dissection, venous thrombosis)
Drug toxicity
Infection (meningitis, encephalitis)
Intracranial tumor
Intracranial hypotension
Metabolic derangements
Primary headache syndromes (benign thunderclap headache, migraine, cluster headache)
Hypertensive disorders

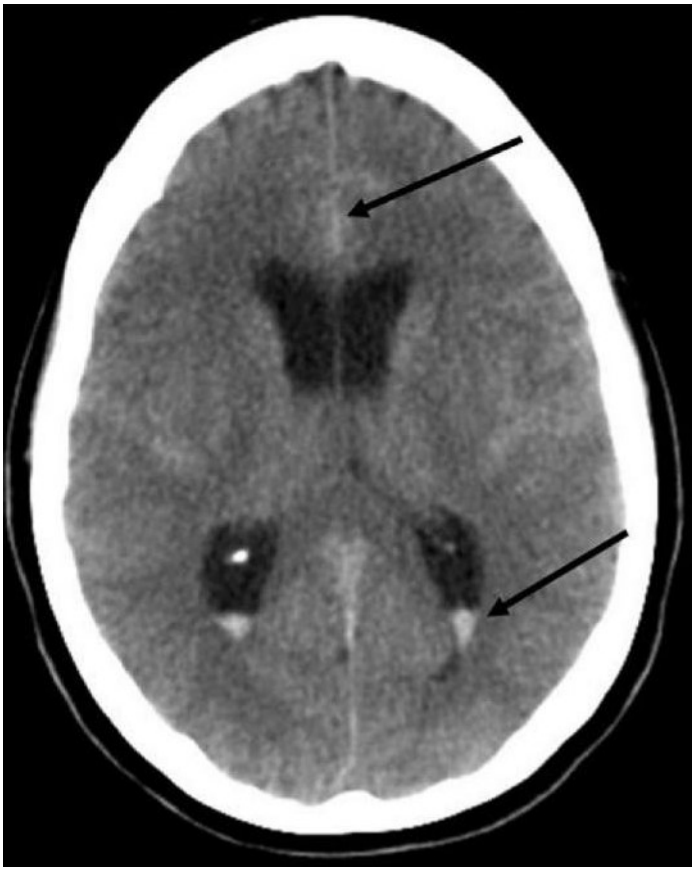

FIGURE 166-1. Diffuse subarachnoid hemorrhage with associated ventricular hemorrhage. *Top arrow* indicates blood in interhemispheric fissure. *Bottom arrow* indicates blood in lateral ventricle. [Image used with permission of James Anderson, MD, Department of Radiology, Oregon Health & Science University.]

Important consequences of this diagnostic pathway include the detection of incidental aneurysms, as opposed to clinically significant bleeds, with the background incidence of aneurysms in the population (2% to 6%) exceeding that of the morbidity and mortality associated with subarachnoid hemorrhages.[16] The major disadvantage of CT/CTA is ionizing radiation. The usefulness of MRI, particularly fluid-attenuated inversion recovery MRI sequences, is limited.[17] A negative MRI result would still need to be followed by an LP.[18] The major disadvantages of MRI/MRA at this time are availability, time to perform the examination, and cost.

Lumbar Puncture Most authorities recommend CSF analysis when a patient with suspected subarachnoid hemorrhage has a normal result on head CT.[19,20] Another advantage of LP is the ability to identify other causes of headache such as meningitis or idiopathic intracranial hypertension. The disadvantages of LP include post-LP headache and inability to perform the procedure in the patient with coagulopathy or thrombocytopenia.

The two CSF tests of greatest interest are the presence of xanthochromia and RBC count. **Xanthochromia** is a yellow appearance of the CSF due to the enzymatic breakdown of blood releasing bilirubin. Any exposure of the CSF to light prior to interpretation can increase the rate of bilirubin degradation, which decreases any xanthochromia present.[1] Similarly, a delay in processing the CSF specimen may result in the development of xanthochromia following a traumatic LP. CSF is evaluated for xanthochromia with visual inspection, the standard technique in most U.S. laboratories, or by spectrophotometry, which may have superior sensitivity but approximately 75% specificity, resulting in additional unnecessary diagnostics for false positives.[21] The utility of the

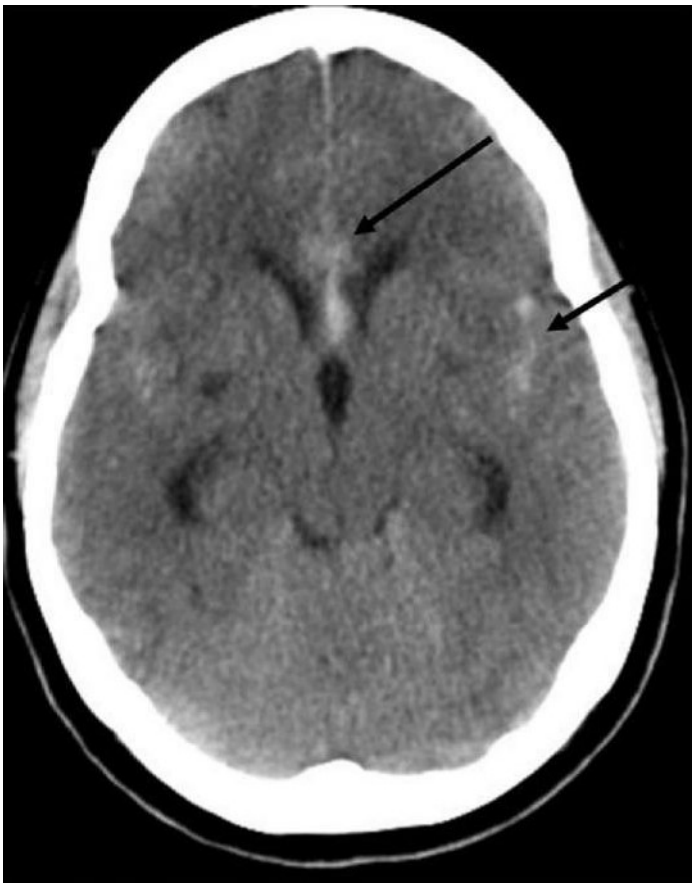

FIGURE 166-2. Scattered subarachnoid hemorrhages (*arrows*). [Image used with permission of James Anderson, MD, Department of Radiology, Oregon Health & Science University.]

test is further limited in that it takes approximately 12 hours for xanthochromia to develop in CSF.[22]

The RBC count in the third or fourth tube of CSF is commonly used to identify subarachnoid hemorrhage. Several issues can make interpreting CSF results challenging. The number of RBCs that constitutes a "positive" LP result has never been clearly defined, nor has the number of RBCs that may be attributed to a "traumatic" LP. One study showed that approximately 10% or 15% of LPs are traumatic, using cutoffs of 400 and 1000 RBCs, respectively.[23] A comparison of cell counts between consecutive tubes or between tubes 1 and 4 is sometimes used to differentiate subarachnoid hemorrhage from a traumatic LP. A small study, however, demonstrated that a 25% reduction in RBCs between tubes 1 and 4 may occur even in cases of confirmed subarachnoid hemorrhage.[24] Another small study found that RBCs <100 in the final tube effectively ruled out subarachnoid hemorrhage, whereas an RBC count of >10,000 in the final tube was associated with an increase in the odds of subarachnoid hemorrhage by a factor of 6.[25]

In general, **normal findings on head CT, the absence of xanthochromia, and zero or few RBCs ($<5 \times 10^6$ RBCs/L) in the CSF help reliably exclude subarachnoid hemorrhage**.[26] A normal head CT result with a positive finding of xanthochromia or elevated RBC count should be considered diagnostic of subarachnoid hemorrhage. **Unfortunately, the literature remains unclear on the precise threshold number of RBCs needed in the CSF to be considered diagnostic of subarachnoid hemorrhage.**

Subarachnoid Hemorrhage Grading Scales Many different subarachnoid hemorrhage grading scales exist. Those most widely used include the Hunt and Hess scale and the World Federation of Neurosurgical Societies scale (**Table 166-3**). A higher grade on either scale indicates a higher likelihood of poor outcome.

TREATMENT

Medical management of the subarachnoid hemorrhage patient in the ED should occur in a monitored critical care area and should target the prevention of complications. Check the Glasgow Coma Scale and pupillary responses regularly because a decrease of 1 Glasgow Coma Scale point can indicate the onset of complications.[1] Intracerebral and extracerebral complications of subarachnoid hemorrhage include rebleeding, vasospasm, cerebral infarction, cerebral edema, hydrocephalus, intracranial hypertension, fluid status and electrolyte abnormalities, respiratory failure, myocardial dysfunction, thromboembolism, and sepsis.[27]

The risk of rebleeding is greatest in the first 24 hours and can be reduced by adequate blood pressure control; however, the ideal target blood pressure and antihypertensive agent remain unclear. If known, maintain the patient's prehemorrhage blood pressure; otherwise, a mean arterial pressure of <140 mm Hg is a reasonable target while avoiding hypotension.[28] Because blood pressure may fluctuate through the course of the disease, a titratable IV antihypertensive is preferred. **Labetalol** and **nicardipine** are most often used, with neither showing clear superiority. **Avoid nitroprusside and nitroglycerin** because they increase cerebral blood volume and intracranial pressure.[29,30] Pain medications and antiemetics also play an important role in maintaining the alert patient's comfort and blood pressure. There is debate regarding the use of antifibrinolytics to prevent rebleeding after subarachnoid hemorrhage, with evidence supporting short- but not long-term use, although generally, these are not used because there is a risk of increased cerebral ischemia.[31]

Vasospasm is most common 2 days to 3 weeks after subarachnoid hemorrhage. A modest protective benefit is seen with administration of nimodipine, 60 milligrams PO every 4 hours, and this therapy should be initiated within 96 hours of symptom onset unless contraindicated due to allergy, nonfunctioning GI tract, or hepatic disease. Clinical trials of other novel treatments, including statins, magnesium, and endothelin receptor antagonist, have not demonstrated significant reductions in mortality.[32-36]

Delayed cerebral ischemia is associated with hypothermia, hyperthermia, and hyperglycemia. Prevent these conditions with the appropriate use of warming or cooling blankets, antipyretics, or insulin when indicated.

TABLE 166-3 Grading Scales for Subarachnoid Hemorrhage

Grade	Hunt-Hess Scale	World Federation of Neurosurgical Societies Scale
1	Mild headache, normal mental status, no cranial nerve or motor findings	GCS of 15, no motor deficits
2	Severe headache, normal mental status, may have cranial nerve deficit	GCS of 13 or 14, no motor deficits
3	Somnolent, confused, may have cranial nerve or mild motor deficit	GCS of 13 or 14, with motor deficits
4	Stupor, moderate to severe motor deficit, may have intermittent reflex posturing	GCS of 7–12, with or without motor deficits
5	Coma, reflex posturing or flaccid	GCS of 3–6, with or without motor deficits

Abbreviation: GCS = Glasgow Coma Scale score.

(*Source:* Reproduced with permission from Hemphill JC: Neurologic critical care, in Fauci AS, Braunwald E, Kasper DL, et al (eds): *Harrison's Principles of Internal Medicine, 17th ed.* © McGraw-Hill Inc., New York, 2008.)

Approximately 5% to 20% of patients with subarachnoid hemorrhage have at least one seizure. Consideration of seizure prophylaxis is currently supported by several clinical guidelines; however, this topic remains controversial and should be determined in conjunction with the intensivist or neurosurgeon who will manage the patient.[37]

DISPOSITION AND FOLLOW-UP

Admit all patients diagnosed with subarachnoid hemorrhage to an intensive care unit in consultation with a neurosurgeon. In the absence of another indication for admission, patients who have normal findings on head CT and CSF analysis within 2 weeks of occurrence of initial symptoms may be safely discharged from the ED.[1,38] Consider consultation with a neurosurgeon for patients who present >2 weeks after the sudden onset of a severe headache causing suspicion for subarachnoid hemorrhage if the initial workup yields normal findings.[1]

INTRACEREBRAL HEMORRHAGE

EPIDEMIOLOGY

Spontaneous intracerebral hemorrhage causes 8% to 11% of all acute strokes and is twice as common as subarachnoid hemorrhage. Like subarachnoid hemorrhage, intracerebral hemorrhage carries a high morbidity and mortality. Seven-day mortality is approximately 30%, 1-year mortality about 55%, and 10-year mortality approximately 80%.[39] Among those who survive, only one in five will be functionally independent at 1 year. There has been no recent change in mortality after intracerebral hemorrhage. This may be because the increased use of anticoagulation for atrial fibrillation to prevent ischemic stroke contributes to poorer outcomes in those patients taking anticoagulants who develop intracerebral hemorrhage.[39] Intracerebral hemorrhage occurs more than two times more frequently in blacks than in whites, which may be related to the higher prevalence of hypertension in blacks.[40] Anticoagulation with warfarin is a significant risk factor for intracerebral hemorrhage, with an annual intracerebral hemorrhage incidence of 0.3% to 0.6% in those taking the drug, and plays a role in 6% to 16% of all cases of intracerebral hemorrhage. Among patients taking warfarin, the risk of intracerebral hemorrhage nearly doubles for each 0.5 increase in international normalized ratio above 4.5. Intracerebral hemorrhage occurs in approximately 3% to 9% of patients treated with tissue plasminogen activator for acute ischemic stroke.[28] Current information suggests that major bleeding events occur at a similar rate with warfarin and direct thrombin inhibitors.[41]

PATHOPHYSIOLOGY

Risk factors for intracerebral hemorrhage include long-standing hypertension, arteriovenous malformations, arterial aneurysm, anticoagulant therapy, use of sympathomimetic drugs (particularly cocaine and phenylpropanolamine), intracranial tumors, and amyloid angiopathy in the elderly. Current smoking and increased frequency of smoking also raise the risk of intracerebral hemorrhage, but the etiology of this increased risk has not been as well defined as in ischemic stroke.[42]

CLINICAL FEATURES

Intracerebral hemorrhage may be clinically indistinguishable from cerebral infarction, subarachnoid hemorrhage, and ischemic stroke. In intracerebral hemorrhage, headache, nausea, and vomiting often precede the neurologic deficit, and in contrast to subarachnoid hemorrhage, the headache onset is usually more insidious. **In hypertensive intracerebral hemorrhage, bleeding is usually localized to the putamen, thalamus, pons, or cerebellum (in decreasing order of frequency)**, and clinical examination findings may be relatable to those areas. **Cerebellar hemorrhage** is commonly associated with dizziness, vomiting, marked truncal ataxia, gaze palsies, and depressed level of consciousness. Patients with cerebellar hemorrhage are more likely to have rapidly progressive symptoms and may require more aggressive intervention than patients with other forms of intracerebral hemorrhage.

DIAGNOSIS AND IMAGING

The differential diagnosis of intracerebral hemorrhage is similar to that of subarachnoid hemorrhage. The history, rapidity of progression of symptoms, and other clinical features may suggest that intracerebral hemorrhage is more likely than subarachnoid hemorrhage or ischemic stroke, but these features are not adequate alone to make a clinical diagnosis. CT and MRI each have areas of superiority in evaluating a patient for intracerebral hemorrhage. **CT is optimal for demonstrating hemorrhage extension into the ventricles, whereas MRI is superior for demonstrating underlying structural lesions.** Either modality is considered acceptable as the initial study for diagnosing intracerebral hemorrhage.[28] Widespread availability of CT makes a noncontrast CT the initial study of choice in most EDs (**Figure 166-3**). The addition of contrast may allow identification of masses or aneurysms.

Cerebral angiography may be useful in selected patients in stable condition who do not require urgent surgery, particularly those in whom no obvious cause of bleeding is identified and those younger than 45 years of age without hypertension.[43]

Additional tests should be performed to exclude coexisting pathology or facilitate surgery, if necessary, including a complete blood count, electrolyte levels, creatinine level, glucose level, electrocardiogram, chest radiograph,

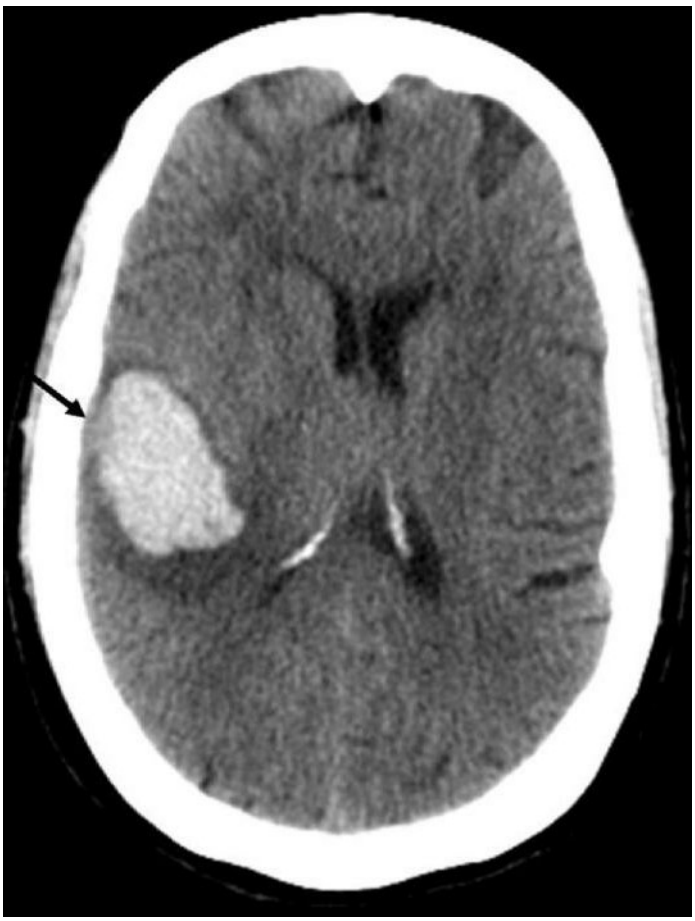

FIGURE 166-3. Large right-sided parietal intraparenchymal hemorrhage (*arrow*). [Image used with permission of James Anderson, MD, Department of Radiology, Oregon Health & Science University.]

TABLE 166-4 Suggested Guidelines for Treating Elevated Blood Pressure in Spontaneous Intracranial Hemorrhage

Clinical Circumstances	Management
SBP >200 mm Hg or MAP >150 mm Hg	Consider aggressive reduction of blood pressure with continuous IV infusion.
SBP >180 mm Hg or MAP >130 mm Hg and evidence or suspicion of elevated ICP	Consider monitoring ICP and reducing blood pressure using intermittent or continuous IV medications to keep cerebral perfusion pressure >60–80 mm Hg.
SBP >180 mm Hg or MAP >130 mm Hg and no evidence or suspicion of elevated ICP	Consider a modest reduction of blood pressure (e.g., MAP of 110 mm Hg or target blood pressure of 160/90 mm Hg) using intermittent or continuous IV medications.

Abbreviations: ICP = intracranial pressure; MAP = mean arterial pressure; SBP = systolic blood pressure.

coagulation studies, and blood type and screen. A urine pregnancy test and screen for drugs of abuse should be performed as appropriate.

TREATMENT

Treatment of patients with intracerebral hemorrhage should occur in a monitored critical-care area with appropriate urgency. Patients with cerebellar hemorrhage are at particularly high risk of rapid deterioration and may require rapid intervention.[44] Maintain close attention to the patient's airway, monitoring of neurologic status, management of hyperthermia with antipyretics, administration of antiepileptic medications if seizures occur, aggressive management of hyperglycemia (>160 milligrams/dL), blood pressure management, and reversal of coagulopathy (if present). Management of elevated intracranial pressure should include raising the head of the bed 30 degrees and providing appropriate analgesia and sedation. If more aggressive reduction of intracranial pressure is required—such as administration of osmotic diuretics or intubation with neuromuscular blockade and mild hyperventilation—invasive intracranial pressure monitoring is generally indicated. Current guidelines for blood pressure management are listed in **Table 166-4**.[28] **The INTERACT2 study demonstrated no reduction in the rate of death or severe disability among patients assigned to rapid (within 1 hr) reduction of blood pressure to <140 mm Hg; however the study showed better functional outcomes in those with rapid BP reduction**.[45]

Reverse Coagulopathy Given the complexity and variety of antiplatelet and anticoagulation agents in current use, institutional protocols should be available with clear algorithms listing the indications for, and dosing of, reversal agents (**Table 166-5**). If the coagulopathy is related to heparin use, administer protamine at approximately 1 milligram per 100 units of heparin, adjusted based on the time since the heparin was last given. For patients taking warfarin, provide reversal no matter what the value of the international normalized ratio. For further discussion, see chapter 239, Thrombotics and Antithrombotics. Several options exist for reversing warfarin-induced coagulopathy: vitamin K, fresh frozen plasma, recombinant factor VIIa, and prothrombin complex concentrates. Preferred route of administration of vitamin K is the PO route, since IV and SC routes can cause anaphylaxis. Vitamin K takes many hours to be effective. Fresh frozen plasma has a faster onset but contains variable amounts of clotting factors, and the dose of 15 mL/kg requires a large volume infusion that most patients cannot tolerate. **Fresh frozen plasma can be available for rapid administration as universal donor (AB+) without the need for type and cross-match.**

Recombinant factor VIIa does not improve survival or functional outcome after intracerebral hemorrhage.[46] **Prothrombin complex concentrates** are effective and rapidly reverse oral anticoagulants; however, morbidity and mortality remain high even when the coagulopathy is reversed.[47]

TABLE 166-5 Reversal of anticoagulation for Intracerebral Hemorrhage

Anticoagulant	Reversal Agent	Comment
Warfarin	Vitamin K 2.5–5 milligrams PO	Full effect in 24 h; IV can cause anaphylaxis; allergic reactions also reported with IM and SC dosing
	Fresh frozen plasma 2 units IV	Full dose 15 mL/kg limited by volume
	Prothrombin complex concentrate (PCC) 50 IU/kg IV	Dose-related risk of thromboembolism; available as 3- (II, IX, X) and 4- (II, VII, IX, X) factor PCC; use what is available in your institution
Aspirin and adenosine diphosphate receptor agonists	Obtain consultation if available when considering platelet infusion	CAUTION: platelet reversal may cause coronary or arterial thrombosis; use only if benefits outweigh risk
Unfractionated heparin (UFH)	1 milligram protamine/100 units of UFH; maximum dose, 50 milligrams; calculate last 3 h of heparin dose to determine protamine dose because heparin has short half-life	Infusion rate ≤5 milligrams/min; risk of hypersensitivity in patients with fish allergy or prior protamine exposure: premedicate with hydrocortisone 500 milligrams IV and diphenhydramine 50 milligrams IV
Low-molecular-weight heparin (LMWH)	If last dose within 8 h, give 1 milligram protamine/1 milligram LMWH; maximum dose, 50 milligrams If last dose 8–12 h ago, give 0.5 milligram protamine/1 milligram LMWH If last dose ≥12 h ago, do not give protamine	See above protamine cautions. Infusion rate ≤5 milligrams/min; higher infusion rates can cause hypotension or bradycardia
Direct thrombin inhibitor or factor Xa inhibitors	No effective reversal agent	Consult hematology While activated charcoal 1 gram/kg can bind apixaban, rivaroxaban, or dabigatran if these drugs were taken in last 2 h, risk of CNS deterioration and pulmonary aspiration typically prohibit use in CNS bleed

Manage intracerebral hemorrhage related to fibrinolytic therapy with standard intracerebral hemorrhage treatment along with platelet and cryoprecipitate infusions, although little evidence exists to guide therapy in these cases.[28]

DISPOSITION AND FOLLOW-UP

Admit all patients to an intensive care unit in consultation with a neurosurgeon.

REFERENCES

The complete reference list is available online at www.TintinalliEM.com.