Patients presenting with symptoms similar to stroke are a true emergency. Recent estimates from the American Heart Association (AHA) and American Stroke Association (ASA) indicate the US annual stroke burden in excess of 610,000 cases to 795,000 cases. Stroke is the third leading cause of death with an estimated 134,000 cases annually. The emergency medicine (EM) physician must determine whether the acute neurologic deficits represent a transient event or a potential stroke. Get with the Guidelines published by the AHA/ASA, emphasizes the rapid evaluation necessary for recognizing patients with possible stroke syndromes. The results of the European Cooperative Acute Stroke Study III (ECASS III), a prospective study in which patients suspected with ischemic stroke were treated with alteplase (recombinant tissue plasminogen activator [rtPA]), demonstrated benefit of this therapy given up to 4.5 hours after symptom onset. This therapy extends the time window for treatment of ischemic stroke from 3 hours to 4.5 hours. During the evaluation period of a patient presenting with symptoms similar to stroke, the emergency physician must also consider the numerous nonvascular disease processes that present with acute neurologic deficits but are not strokes. These conditions are stroke mimics. Rapid identification of a stroke mimic prevents treatment with thrombolytics and interventional stroke therapies as well as the possible complications from such treatment.
The job of the emergency physician is difficult. The first area of difficulty begins with the type of emergency department (ED) and the availability of resources that the emergency physician has at his/her disposal. Academic EDs that are designated as stroke centers have a stroke team that is activated by the emergency physician. A stroke neurologist is immediately available to assess the patient and a radiologist to interpret the computed tomography (CT) of the head. The stroke neurologist decides on further imaging (CT angiogram or magnetic resonance imaging [MRI]), thrombolysis, or interventional therapy. Academic centers have 24-hour availability of CT angiograms and/or MRI. Interventional capability through either a neurointerventional physician or an interventional radiologist is also available. Alternatively, community and rural hospitals may have only 1 emergency physician working, with or without a neurologist available for telephone consultation. In some rural EDs, night staffing is with physician extenders or physicians who are not trained in EM. Radiology services for interpreting CT studies may be outsourced to radiologists elsewhere in the United States or even abroad. The emergency physician or physician extender in these circumstances must be able to review CT studies and decide on initiating thrombolysis with rtPA. The emergency provider in this setting then has a far more complex role in determining if a stroke mimic exists.

The actual number of patients who present with a stroke mimic compared with those with true stroke varies depending on the research study that deals with this question. A prospectively collected stroke/MRI data bank in Germany from 2004 to 2010, had 42 of 648 (6.5%) patients suspected with ischemic stroke treated with rtPA with a final diagnosis of a stroke mimic. Stroke mimic diagnoses included 20 patients with seizures, 7 patients with conversion disorders, 6 patients with dementia, 3 patients with migraine headache, 2 patients with brain tumors, and 4 other cases. Complications from rtPA therapy occurred in only 1 of the patients in this study (orolingual edema). Chernyshev and colleagues found that 14% of the treated patients were eventually diagnosed with a stroke mimic and none suffered a complication from thrombolytic therapy. This group of patients only included those treated in the 3-hour window from symptom onset.

Little attention has been paid to patients presenting with transient ischemic attacks (TIAs) and conditions mimicking TIA. In a single center, prospective cohort study over 2 years in Switzerland, approximately 20% of patients suspected with TIA at presentation were TIA mimics. This article does not discuss about TIA mimics.

This article describes the common stroke mimic presentations by cause, including toxic-metabolic pathologies, seizure disorders, degenerative neurologic conditions, and peripheral neuropathies. These conditions are not immediately obvious to the treating physician, and he/she has to rely on history taking, laboratory analysis, and neuroimaging studies to elucidate possible stroke mimics. Even with a stroke team comprising a neurologist and neuroradiologist assisting the emergency physician, patients with stroke mimics will not always be immediately identified.

TOXIC-METABOLIC

Glycemic imbalance can present in the form of high or low blood glucose level. Hypoglycemia can be loosely defined as low blood glucose levels with changes in the mental status. The most commonly cited laboratory values for hypoglycemia in diabetics is a blood glucose level of less than 70 mg/dL, with presence of signs or symptoms consistent with low blood glucose level, as well as the resolution of symptoms with the correction of low blood glucose level. Although the correction of hypoglycemia should be accompanied by the resolution of symptoms, neurologic
symptoms may linger somewhat after glucose treatment. In healthy individuals, a level of less than 55 mg/dL of blood glucose has been used as the threshold for hypoglycemia although it can present at lower levels if there have been previous recurrent episodes of hypoglycemia. Patients may exhibit signs and symptoms that may be confused with a cerebrovascular accident when truly presenting with isolated hypoglycemia. As blood glucose level becomes dangerously low, patients may present with confusion, altered behavioral patterns, seizure, and/or coma. Foster and Hart exemplify the focal neurologic deficit in the setting of hypoglycemia with a study of 2 patients with recurrent presentations of hemiplegia. On each presentation, symptoms were corrected with a reduction in insulin dosing and workups including angiography were negative for a primary neurologic event. One study showed a 2% prevalence of hypoglycemic hemiparesis although there was concomitant evidence of vascular disease in these patients. In subsequent reviews, hypoglycemic hemiplegia has been unreliably associated with vascular disease. Right-sided hemiparesis is more common than left sided, and right-sided hemiparesis often has associated aphasia.

Hyperglycemia is also capable of producing focal neurologic deficits. Many patients regularly have an elevated level of blood glucose, but neurologic changes may occur when it becomes pathologic, such as in diabetic ketoacidosis or hyperosmolar hyperglycemic nonketotic state. This condition is more common in patients with nonketotic hyperglycemia in whom metabolic encephalopathy can develop, with involvement of the cortex, brain stem, and spinal cord leading to neurologic signs. Maccario thought focal deficits, including homonymous hemianopsia, hemiplegia, hemisensory deficits, and aphasia, were caused by cellular hyperosmolarity.

Metabolic imbalances, such as hypernatremia, hyponatremia, and hepatic encephalopathy, may also cause focal neurologic deficits. Hypernatremia is similar to hyperglycemia in its effect of cerebral hyperosmolarity and the resultant encephalopathy due to failure of thirst, antidiuretic hormone secretion, and initially slow onset of corrective idiogenic osmoles to abate cellular shrinkage. Hyponatremia causes encephalopathy through cellular swelling, but can be acute or insidious in onset, with acute onset more often associated with neurologic changes. Hepatic encephalopathy has been rarely documented as causing focal neurologic deficits, but in a study by Cadranel and colleagues, 17.4% of patients with hepatic encephalopathy over a 12-month period showed neurologic deficits. This included 48 episodes of encephalopathy due to liver pathology with 8 instances of resolved focal neurologic deficits with the resolution of hepatic encephalopathy. Patients were most commonly found to have hemiparesis and hemiplegia, noted in comatose patients because of decreased movement with painful stimuli. All patients with documented neurologic signs had negative head CT and lumbar puncture, but not all had brain MRI and/or echo Doppler studies of the neck. There was no prognostic significance of patients who did show neurologic deficits versus those who did not in the outcome of the hepatic encephalopathy. These neurologic deficits had not previously been well noted in the literature, but the investigators thought it was important for physicians to be aware of this presentation.

INGESTIONS

Patients presenting with altered mental status and an atypical neurologic examination should raise suspicion for ingestion, including use of illicit drugs, misuse of prescription medications, overdose of any medication, or drug interactions. Toxicologic screening including, but not limited to, salicylates and acetaminophen, as well as
opiates or other illicit drugs capable of sedation or unusual behaviors is essential. An electrocardiogram is essential to assess for cardiac dysrhythmias caused by medications and to check the PR interval and QTc interval for concerning cardiac results of ingestion. Ingestions are a diagnosis of exclusion in the acutely altered patient and should be ruled out while working up the possibility of a true neurologic event.

SEIZURE AND TODD PARALYSIS

Along with hypoglycemia, seizure has been noted as the most common presenting condition resulting in a stroke mimic.8,9 Patients with focal seizures, even if progressing to generalized seizures, can present with hemiparesis, often referred to as Todd paresis; gaze deviation; and decreased mental status. The cause of Todd paresis is attributed to increased metabolic demand from the active depletion of the excitatory neurons in the postictal state.10 Rupprecht and colleagues14 studied postictal dysfunction using cranial perfusion MRI scans and found evidence of early global hemispheric perfusion mismatch without lasting injury. MRI at 10 hours show full resolution, with interval hyperperfusion. Changes are not associated with a particular vascular distribution but rather associated with the epileptic focus and surrounding tissue.11,12

MIGRAINE HEADACHE

Migraine headache is a recurrent throbbing headache, either unilateral or bilateral, that can have a prolonged course with associated visual and auditory irritation, and up to 25% of patients with migraine exhibit focal neurologic deficits.15–17 Migraine has a similar causative function as seizures in the focal neurologic deficit masking as a stroke.13,16 The pathophysiology is termed cortical spreading depression, with the excitation of neurons and subsequent inhibition.13,16,18 One subtype of migraine is the hemiplegic migraine, which can be either sporadic or genetically inherited and is defined by an aura accompanied by motor weakness. They often progress throughout a patient’s lifetime with the gradual worsening of visual, sensory, aphasia, and cerebellar symptoms. Patients diagnosed with hemiplegic migraines may experience headache without these neurologic deficits. Most aspects of the hemiplegic migraine are self-resolving, but in a small number of patients, it causes permanent neurologic changes.18

DEGENERATIVE NEUROLOGIC DISORDERS, MULTIPLE SCLEROSIS, OPTIC NEURITIS

Degenerative neurologic disorders occur in many forms, including multiple sclerosis (MS) and leukoencephalopathy from viruses, medications, or ingestions. The resultant demyelination from these disorders can present with hemiparesis, cranial nerve palsies, and vision disturbances. The most discussed demyelinating disease is MS, in which a small subset of patients suffers from brief paroxysmal symptoms, such as dysarthria, ataxia, diplopia, and sensory deficits, which are a less common feature of disseminated sclerosis.14,19–21 Researchers have found the responsible lesions at the level of the midbrain or below, as shown on MRI scans of patients in the paroxysmal dysarthria-ataxia subgroups.20,22 These attacks are usually well controlled and have a dramatic improvement with carbamazepine.14,20,22,23

A well-described postinfectious or postimmunization cause of demyelination is acute demyelination encephalomyelitis (ADEM),24 which is more common in children, and an immune-mediated process. Differentiation between ADEM and MS has been studied more commonly in children, but ADEM is noted to have a shorter onset of
about 5 days and is monophasic compared with approximately 2 weeks with MS and is chronic. Demyelination has also been noted in patients with JC virus, which has been associated with progressive multifocal leukoencephalopathy, in immunocompromised hosts. Most individuals are carriers by adulthood, up to 80%, but JC virus focus its attack in patients with CD8 + deficiency.

Optic neuritis, which is a demyelinating condition of the optic nerve, may be present bilaterally, but is more commonly unilateral in MS and bilateral in ADEM. Bilateral presentation is also more common in children compared with adults with acute demyelinating optic neuritis. In MS, 15% to 20% of patients initially present with optic neuritis and about 50% of all patients with MS develop optic neuritis at some time. Presentation is often subacute, with loss of red-vision in particular, visual field loss and an afferent papillary defect are often present as well.

Myelopathy is a pathologic condition that affects the spinal cord, leading to motor or sensory loss. Acute myelopathy is defined as having maximum effect within 4 weeks of onset. Causative factors include trauma, compressive lesions, vascular lesions, infection or inflammation, and toxic, paraneoplastic, or electrical injuries. Acute myelopathies are often diagnosed when the patient does not have the hallmark findings of MS, including the typical MRI findings of demyelinating lesions, leading to a broader differential diagnosis. Inflammatory changes of the spinal cord are most commonly due to direct or postinfectious causes and other autoimmune demyelinating diseases, such as ADEM. Inflammatory myelitis can cause acute transverse myelitis, and likely causes include viral, bacterial, postvaccination, and autoimmune diseases; MS; paraneoplastic syndromes; or idiopathic. Bacterial pathogens such as mycoplasma, tuberculosis, Lyme, and syphilis may also lead to myelitis. T. pallidum was the most common cause before the discovery of antibiotics. Symptoms of transverse myelitis include weakness in the legs, increase in pain sensation (allodynia), changes in bowel or bladder control, and, less commonly, sensory changes. Infectious myelopathies are less common, with HIV being the most common cause of infectious myelopathies. Viral causes include herpes simplex and zoster, enteroviruses, human T-cell lymphotropic virus type I, and mycobacterium.

CEREBROVASCULAR NARROWING

The primary causes of cerebrovascular narrowing include central nervous system (CNS) vasculitis, reversible cerebral vasoconstriction syndrome, aneurysmal subarachnoid hemorrhage, and atherosclerosis. Primary CNS vasculitis and reversible cerebral vasoconstriction have similar angiographic findings but are separate entities with differing implications. Vasculitis of the CNS is a rare and poorly understood entity, which was first described in 1959 by Cravioto and Feigin. Since that time, only about 500 cases have been identified. Diagnosis of primary angiitis of the CNS (PACNS) is increasing because of more recent awareness and improved imaging technology, but the case numbers remain small. PACNS is most commonly found in men in the fifth decade of life. Onset of PACNS is variable from acute to chronic and, in some cases, may mimic chronic meningitis. PACNS is usually a multivessel disease affecting varied cerebral territories. Signs and symptoms range from visual changes secondary to cranial nerve involvement to ataxia and myelopathies, often in conjunction with constitutional systemic manifestations. It is estimated that 30% to 50% of patients diagnosed with PACNS ultimately have TIAs and strokes secondary to the vascular changes.

Reversible cerebral vasoconstriction syndrome (RCVS) is characterized by a thunderclap headache and may or may not be associated with neurologic findings. Young
women between the ages of 20 and 50 are most commonly affected and frequently have a past medical history of migraine headaches. There is a small, but significant, morbidity associated with RCVS that may result in ischemic or hemorrhagic stroke. Although a stroke may result from vasoconstriction, this condition being reversible, by its definition, often leaves most patients with few long-term adverse outcomes. There are several subsets of syndromes in RCVS, but the essential finding is vasospasm of the cerebral vessels, resolving over days to weeks. Inciting factors include trauma, hypertension, sympathomimetic drugs, and cerebral tumors. Marijuana, cocaine, nicotine patches, selective serotonin reuptake inhibitors, and nasal decongestants, such as pseudoephedrine and ephedrine, are all associated with RCVS. Neurologic effects from vasoconstriction can vary and involve the brain territory supplied by the constricted artery, causing signs and symptoms, such as dysarthria, hemiplegia, hemisensory deficits, aphasia, visual changes, and more. Hemorrhagic or ischemic stroke has been cited with persistent vasoconstriction and is the major determinant of morbidity and mortality in these patients.

Idiopathic intracranial hypertension (IIH), previously known as pseudotumor cerebri, is a syndrome that often afflicts young, obese women, and is characterized by increased intracranial pressures in the absence of structural cerebral changes including obstruction, mass, vascular lesions or changes in the cerebrospinal fluid (CSF). IIH was initially a “benign” condition, but Corbett and Thompson demonstrated the destructive vision changes caused by papilledema, which lead to a change in the nomenclature from benign intracranial hypertension to IIH. Decreased vision stems from optic atrophy as a direct result of increased intracranial pressure. Approximately 25% of patients with IIH experience such vision disturbances. Patients with IIH most commonly present with headache and often experience visual obscurations and less commonly double vision and blurry vision. Approximately 35% to 70% of patients experience visual symptoms. Abducens nerve is the most commonly affected cranial nerve and was previously included in the presenting signs of IIH according to the Modified Dandy Criteria. The criteria has since been updated by Friedman and Jacobson and VI nerve palsy is no longer explicitly included in the definition but is nonetheless still often present. Occurring in about 80% of cases, IV nerve palsy is caused by increased pressure on the nerve from increased intracranial pressure, causing mass effect. Facial nerve, oculomotor, trochlear, and trigeminal nerve palsies have all been observed infrequently in patients with IIH. Papilledema is present in most patients, but its absence does not exclude the diagnosis of IIH.

PERIPHERAL NEUROPATHIES

Peripheral neuropathies are due to cellular changes in nerves that lie outside the brain, spinal cord, and CNS. These include small to large diameter nerves innervating either motor or sensory systems. Because of their anatomic distribution and placement in proximity to bony foramina and ligamentous spaces, they are susceptible not only to ischemic, toxic or autoimmune damage, but also to bony compression and entrapment. Three main types of degeneration exist including axonal degeneration, segmental degeneration, and wallerian degeneration. Axonal degeneration damages the myelin distally and the axis cylinder. Segmental degeneration has myelin damage but axonal sparing. Wallerian degeneration is from a direct injury to the nerve resulting in distal degeneration due to the separation from the cell body. Main symptoms include motor dysfunction, muscle atrophy, loss of sensation and reflexes, paresthesias, and pain. Neuropathies include mononeuropathies, polyneuropathies,
radiculopathies, and plexopathies, which involve multiple nerves within a plexus. The vast networks of peripheral neurons mean there is a multitude of neural pathologic condition. These can be differentiated from the pathologic conditions of the CNS through physical examination, radiological imaging of the brain, electromyography, nerve biopsy, and CSF and blood testing. Often, this extent of testing requires more time than an initial emergency department visit to make such a diagnosis with certainty. Guillain-Barre Syndrome is an ascending paralysis that is divided into several subtypes characterized by symmetric peripheral weakness, areflexia, increased protein levels in the CSF and a progressive ascending course of motor weakness.

**SUMMARY**

Stroke mimics are an important consideration for emergency physicians and physician extenders working in EDs. Even with a time window of 4.5 hours, the work-up must often be accelerated depending on the time at which the patient presents to the ED. As previously noted, the resources available to emergency providers differ greatly across the country. Nevertheless, it is incumbent on the emergency provider to think stroke first and proceed accordingly.

**REFERENCES**