Question 1

A 42-year-old man is evaluated in the emergency department for a 1-week history of bilateral leg weakness and numbness. He has an 8-year history of multiple sclerosis (MS) that is currently well controlled with natalizumab; he has had no MS exacerbations since beginning treatment 2 years ago after unsuccessful trials of interferon beta and glatiramer acetate. The patient also has chronic fatigue and depression. Medications are monthly natalizumab, twice daily amantadine and extended-release bupropion, a daily multivitamin, and a calcium–vitamin D supplement that he rarely takes.

On physical examination, temperature is 36.7 °C (98.1 °F), blood pressure is 124/58 mm Hg, pulse rate is 74/min, and respiration rate is 14/min. Muscle strength is 4/5 in the bilateral hip flexors, knee flexors, and foot dorsiflexors. Decreased pinprick sensation is noted just below the umbilicus.

Laboratory studies performed 3 weeks ago showed no evidence of elevated serum antibody titers against the JC virus. Results of current complete blood count, liver chemistry studies, and a urinalysis show no abnormalities.

An MRI of the brain shows white matter hyperintensities consistent with MS and is unchanged from an MRI obtained 1 year ago.

In addition to a 5-day infusion of intravenous methylprednisolone, which of the following is the most appropriate next step in management?

13%

A
Discontinuation of natalizumab

15%

B
Measurement of serum 25-hydroxyvitamin D level

71%

C
MRI of the lumbar spine

1%

D
Oral trimethoprim-sulfamethoxazole for 5 days

Answer & Critique

Correct Answer: B

Educational Objective: Diagnose vitamin D deficiency in a patient with multiple sclerosis.

Key Point

Vitamin D supplementation as an adjunctive treatment in multiple sclerosis (MS) has been shown to be superior to disease-modifying therapy alone and has become a standard of care for patients with MS, especially those who are vitamin D deficient.

This patient's serum 25-hydroxyvitamin D level should be measured. He most likely has experienced a breakthrough relapse of multiple sclerosis (MS), which should be treated with intravenous methylprednisolone. Given his 2 years without relapses, the MS is relatively well-controlled. However, his care is not fully optimized because he rarely takes the vitamin D supplement. Accumulating evidence suggests that disease activity in MS is highly linked with serum vitamin D levels, with less frequent relapses and fewer new MRI lesions in patients with higher levels. This patient's serum 25-hydroxyvitamin D level should thus be measured to determine if he is vitamin D deficient. Vitamin D supplementation as an adjunctive treatment in MS has been shown to be superior to disease-modifying therapy alone and has become a standard of care for MS patients, especially those who are vitamin D deficient, although the ideal dosing regimen and serum 25-hydroxyvitamin D level are still unknown. Pharmacodynamic studies are under way that may help inform dosing regimens. Vitamin D supplementation also protects against osteoporosis, for which patients with MS are at higher risk.

This patient has no clear indications supporting discontinuation of natalizumab at this time. Natalizumab is the most highly effective drug for MS currently available, which is borne out by his relapse-free status for 2 years and stable brain MRI results. Although this drug is sometimes associated with progressive multifocal leukoencephalopathy (PML), his recent negative result on JC virus antibody testing place him at a very low risk for development of PML, and the spinal cord localization of this current relapse also argues against PML, which does not affect the spinal cord.

The bilateral leg weakness and sensory level around the umbilicus (T10) are consistent with localization to the thoracic spinal cord. Therefore, an MRI of the lumbar spine would not be appropriate.

This patient has no indication for antibiotic therapy, which makes a 5 -day course of trimethoprim-sulfamethoxazole inappropriate.

Question 2

A 67-year-old woman is evaluated for a 1-year history of increasing forgetfulness. She reports greater difficulty keeping track of upcoming appointments, recalling details of recent telephone conversations, and remembering names of new acquaintances. She has completed 16 years of formal education, currently works as a teacher's assistant, and has noticed no change in her ability to perform classroom duties, including carrying out the instructions of the teachers with whom she works. The patient lives alone and is able to care for her self, drive, and manage her finances. She describes her mood as “upbeat,” continues to enjoy her life, and has had no other symptoms. She does not take any medication.

On physical examination, vital signs are normal. All other physical examination findings , including those from a neurologic examination, are normal. She scores 24/30 on the Montreal Cognitive Assessment, losing points in the orientation and delayed recall sections.

Which of the following is the most likely diagnosis?

A
Dementia

B
Depression

C
Mild cognitive impairment

D
Normal aging

Answer & Critique

Correct Answer: C

Educational Objective: Diagnose mild cognitive impairment.

Key Point

A score lower than 26/30 on the Montreal Cognitive Assessment generally suggests cognitive impairment, especially in patients with many years of formal education.

The most likely underlying cause of this patient's symptoms is mild cognitive impairment (MCI). MCI is a cognitive state between normal aging and dementia characterized by a decline in cognitive functioning that is greater than what is expected with normal aging but has not resulted in significant functional disability. For most patients, the onset is insidious, and for some, the course may be progressive; 10% to 15% of patients with MCI transition to dementia per year, compared with 1% to 2% per year of the general population. The Montreal Cognitive Assessment is a screening tool that is more sensitive than the Mini–Mental State Examination in the detection of MCI because it has more cognitively challenging tests of memory/recall and executive function. A score lower than 26/30 generally suggests cognitive impairment, especially in patients with 16 years of formal education. In clinical practice, a careful history and results of a standard mental examination are often sufficient to make a diagnosis of MCI, and extensive cognitive testing is not routinely required. Occasionally, a formal battery of neuropsychological testing beyond the standard mental examination is needed to distinguish particularly mild cases of cognitive impairment from normal aging.

In order to meet criteria for dementia, a patient's cognitive deficits must interfere with daily functioning and result in some loss of independence. A detailed history of the patient's abilities to perform activities of daily living, such as paying bills, managing financial records, assembling tax records, shopping alone, working on hobbies, taking medications, driving, and remembering recent holidays or family events, should be obtained to elicit any change in function. This patient does not meet the criteria for dementia.

The diagnosis of clinical depression is based on patient history and exclusion of alternative diagnoses; no additional tests can confirm the diagnosis. The evaluation must establish whether

the patient meets established criteria for major depression, dysthymia, or a different psychiatric condition and also assess for substance abuse. Depressed mood and anhedonia are cardinal symptoms, and the presence of either is highly sensitive but not specific for major depression. Using a two-item questionnaire that assesses for the presence of depressed mood or anhedonia is a quick way to screen for depression. If either depressed mood or anhedonia is present, further inquiry or employing a second tool to diagnose depression should be pursued. This patient, who describes her mood as upbeat and says she enjoys her life, has neither depressed mood nor anhedonia. Therefore, depression is unlikely to be the cause of her symptoms.

Patients with memory problems due to normal aging have symptoms, most notably memory loss, that are commonly associated with cognitive impairment, but cognitive testing shows functioning within the normal range. This patient's memory difficulties are greater than what is expected with normal aging, and her score on the Montreal Cognitive Assessment is not in the normal range.

Question 3

A 35-year-old man is evaluated in the emergency department for a 7-hour history of midback pain and bilateral leg numbness. He was in a bar fight immediately before symptom onset and sustained forceful kick injuries to the back, head, and limbs; he did not lose consciousness.

On physical examination, temperature is 36.6 °C (97.8 °F), blood pressure is 110/70 mm Hg, pulse rate is 108/min, and respiration rate is 18/min; BMI is 32. The patient is alert without any apparent cognitive deficits. Lacerations on the face, scalp, and extremities are noted, as are hematomas on the midback and chest. No tremors or significant swelling or hematomas on the scalp are detected. Muscle strength is 3/5 in the lower extremities, and muscle tone in the legs is reduced. Muscle tone in the arms is normal, and anal sphincter tone is reduced. Pinprick testing shows a sensory level below T8.

Which of the following is the most appropriate next step in management?

A
CT of the head

B
High-dose methylprednisolone

C
MRI of the thoracic spine

D
Phenytoin

Answer & Critique

Correct Answer: B

Educational Objective: Treat acute spinal cord injury.

Key Point

High-dose methylprednisolone administered within 8 hours of a traumatic spinal cord injury has been shown to improve motor function recovery.

This patient should receive high-dose methylprednisolone as the next step in management. He has an acute spinal cord injury most likely due to traumatic fracture of a thoracic vertebra and subsequent spinal cord compression. The localization of the injury at approximately the T8 level of the spinal cord is clear, given the bilateral leg weakness and reduced tone, reduced anal sphincter tone, and the sensory level on pinprick testing. Large clinical trials have shown improved motor function recovery up to 1 year after administration of an intravenous bolus of methylprednisolone, 30 mg/kg, within the first 8 hours of traumatic spinal cord injury followed by a 5.4-mg/kg infusion over the next 23 hours. A recent trial has shown that extending this infusion for an additional 24 hours further increases recovery. Because of these studies, immediate administration of high-dose methylprednisolone for suspected traumatic spinal cord injury has become standard of care.

Diagnostic studies are not appropriate because of the acuity of the situation. Given that the patient experienced the trauma 7 hours before he was seen in the emergency department, ordering CT or MRI would delay initiation of treatment, which is necessary within the first 8 hours of the traumatic event. Obtaining a confirmatory MRI of the thoracic spine at a later time is appropriate. However, CT of the head is not needed because the injury localizes to the thoracic spine on examination. Although the patient received some trauma to the head, CT is likely unnecessary, given that he had no loss of (or impaired) consciousness, no evidence of significant external head trauma, and no other signs or symptoms of traumatic brain injury.

Phenytoin would not treat this patient's spinal cord injury. Administration of phenytoin after significant head trauma may be indicated to prevent seizures, but this patient does not appear to have significant head trauma, nor is this the most acute issue at this time.

Question 4

A 55-year-old man is evaluated in the emergency department for a 20-minute episode of left eye visual loss without pain followed by a 5-minute episode of slurred speech. He has no residual symptoms. The patient has hypertension treated with amlodipine. He takes no other medication.

On physical examination, blood pressure is 178/92 mm Hg, pulse rate is 78/min and regular, and respiration rate is 12/min. Carotid upstrokes are normal without bruits. Heart rate is regular, and no murmurs are heard. Other physical examination findings, including those from a neurologic examination, are normal.

Findings on an electrocardiogram and a noncontrast CT scan of the head are normal.

Which of the following is the most appropriate next diagnostic test?

A
Carotid ultrasonography

B
CT angiography of the neck

C
MRI of the brain

D
Transesophageal echocardiography

Answer & Critique

Correct Answer: A

Educational Objective: Evaluate transient ischemic attack.

Key Point

In a patient with a suspected transient ischemic attack, noninvasive carotid ultrasonography is the most appropriate test to exclude significant atherosclerotic disease.

The patient should undergo carotid ultrasonography. He most likely has experienced a transient ischemic attack (TIA), which implies the absence of retinal or cerebral infarction. His $ABCD^2$ score, which is based on a patient's Age, Blood pressure, Clinical presentation, Duration of symptoms, and the presence of Diabetes mellitus, is 2 (one point for elevated blood pressure and one point for the symptom of slurred speech), which indicates a 2-day stroke risk of 1.3%. The antecedent transient monocular blindness in the left eye is concerning for extracranial atherosclerosis of the internal carotid artery. Hospital admission is recommended for all patients with TIAs who have an $ABCD^2$ score of 3 or greater to expedite diagnostic testing and stroke subtyping; admission is also recommended for patients with a score of 0 to 2 if rapid outpatient evaluation cannot be performed.

Carotid ultrasonography to evaluate for symptomatic extracranial internal carotid artery stenosis is the most appropriate next diagnostic test in this patient with a TIA, given the high risk of early recurrence. Patients with greater than 70% extracranial internal carotid artery atherosclerotic stenosis have the highest risk of stroke in the 2 weeks after a TIA. Carotid Duplex ultrasonography is noninvasive and can effectively rule out significant atherosclerotic disease. If the ultrasound suggests greater than 50% stenosis, hospital admission and a confirmatory test with magnetic resonance or CT angiography is appropriate, with plans for early revascularization. Rapid cardiac testing with transthoracic echocardiography and cardiac rhythm evaluation also is advised within 24 hours for all patients with suspected TIA, as is vascular imaging of the extracranial carotid arteries.

CT angiography of the neck is inappropriate at this point because extracranial internal carotid artery stenosis can be excluded without exposing the patient to a highly invasive procedure with contrast and radiation.

Although an MRI of the brain can distinguish a TIA from an ischemic stroke and reveal infarcts in other arterial territories, it is inappropriate as the next diagnostic test in this patient because results are unlikely to affect immediate management. In addition, MRI may not be readily available and may be contraindicated in some patients.

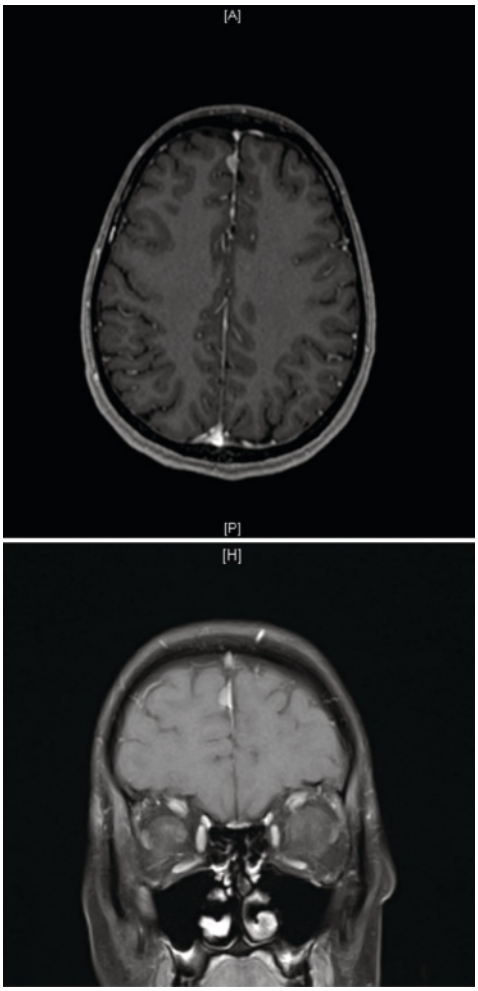
Transesophageal echocardiography may be indicated to identify embolic sources of a TIA or stroke in patients in whom noninvasive diagnostic testing has been unrevealing. However, the yield of transesophageal echocardiography is low (approximately 1%) in patients who are in sinus rhythm, particularly among those older than age 45 years. Although MRI ultimately may be indicated for this patient, appropriate noninvasive testing should be performed first, including cardiac rhythm evaluation and vascular imaging of the carotid arteries.

Question 5

A 42-year-old man comes to the office to discuss results of imaging studies, which were ordered because of a change in his pattern of chronic migraine. Headache episodes have now improved.

On physical examination, temperature is normal, blood pressure is 110/80 mm Hg, pulse rate is 80/min, and respiration rate is 16/min. All other findings from the general physical and neurologic examinations are normal.

A noncontrast CT scan of the head shows a hyperintense extra-axial lesion located between the frontal lobes (parafalcine), which is confirmed by the axial (*top*) and coronal (*bottom*) MRIs shown.



Which of the following is the most appropriate next step in management?

A

Lumbar puncture

B

Radiation therapy

C

Repeat MRI in 3 to 6 months

D **Surgical resection**

Answer & Critique

Correct Answer: C

Educational Objective: Monitor an incidentally discovered meningioma.

Key Point

Meningiomas have characteristic imaging features, including intense homogeneous contrast enhancement (“lightbulb sign”) and a dural tail.

Repeat MRI in 3 to 6 months is the most appropriate next step in management. The radiographic features associated with this patient are most consistent with a meningioma, which may be unrelated to his previous headaches, given the tumor's small size and lack of other symptoms. Meningiomas are benign tumors that arise from the meningeal coverings of the brain. They are the most common extra-axial (not in the brain parenchyma) intracranial lesion in adults. Meningiomas are typically slow-growing tumors, and clinical signs tend to be subtle. They also are often discovered incidentally, as in this patient. Meningiomas have characteristic imaging features, including intense homogeneous contrast enhancement (“lightbulb sign”), areas of calcification, and a dural tail, which is thickening of the dura adjacent to the mass. Patients with small, asymptomatic meningiomas without evidence of invasion of other intracranial structures and without surrounding edema are usually followed clinically and radiographically. Meningiomas should be monitored for growth, with a first follow-up scan performed 3 to 6 months after they are identified.

Lumbar puncture is not indicated in this patient whose imaging findings are characteristic of a meningioma. Lumbar puncture may be indicated in patients with suspicious imaging findings (such as partial enhancement or ring enhancement) suggestive of an infectious or inflammatory process. Lumbar puncture is only appropriate in these patients if they also have evidence of increased intracranial pressure, such as papilledema.

Patients with symptomatic tumors, tumors that invade surrounding parenchyma, or tumors that grow over time may be considered for surgery and/or radiation therapy. If intervention is indicated, surgical intervention is usually the first-line therapy, followed by radiation for higher grade tumors or tumors that could not be resected completely. These treatments are not appropriate at this time in this patient who has none of these indications.

Question 6

A 39-year-old woman is evaluated in the emergency department 45 minutes after having a seizure witnessed by her husband. The seizure, which occurred 10 minutes after she awoke this morning, lasted 90 seconds; she reports now being “back to normal.” According to her husband, the seizure was characterized by a loud cry and unilateral stiffening and shaking. She has no memory of the seizure but does recall an intense feeling of déjà vu just before losing consciousness; she reports that she has had a similar sensation lasting 5 to 15 seconds several times over the past few years. She had been at a birthday celebration the night before her seizure, had several alcoholic drinks, and stayed out late, which is unusual for her. She says she fell on ice 1 month ago, striking her head; except for a mild headache that lasted for several days after the fall, she has had no residual symptoms. She has no other significant medical history and takes no medication.

On physical examination, temperature is 37.2 °C (99.0 °F), blood pressure is 120/70 mm Hg, pulse rate is 95/min, and respiration rate is 14/min. All other findings from the general physical and neurologic examinations are unremarkable.

Results of laboratory studies are normal, including a blood ethanol level of 0.

Which of the following is the most likely diagnosis?

A
Alcohol withdrawal seizure

B
Focal epilepsy

C
Generalized epilepsy

D
Posttraumatic seizure

Answer & Critique

Correct Answer: B

Educational Objective: Diagnose focal epilepsy.

Key Point

Evaluating a patent with an apparent first seizure should include direct questioning about previous subtle events, such as auras, changes in awareness, and periods of inattention, that may indicate the presence of an as yet unrecognized epilepsy syndrome.

This patient most likely has a focal epilepsy syndrome. It is crucial to ask a patient being evaluated for a first seizure about previous more subtle events, such as auras, changes in awareness, and periods of inattention, that may indicate the presence of an as yet unrecognized epilepsy syndrome. The difficult-to-describe sensation of déjà vu that occurred just before this patient's seizure most likely represents an epileptic aura, which is actually a simple partial seizure. The fact that she had the same sensation previously over the past several years suggests that she has had partial seizures before. The features of her current seizure (unilateral shaking and a subjective aura before the onset of convulsion) suggest progression to a secondarily generalized seizure typical of focal epilepsy, although these features are not always present in secondarily generalized seizures.

Alcohol withdrawal is among the many metabolic stressors that can lead to a provoked seizure. Alcohol withdrawal seizures typically occur with other symptoms of withdrawal (behavioral changes and autonomic symptoms) but can sometimes occur in isolation before other withdrawal symptoms. This type of seizure typically does not have the focal features described in this patient, whose previous, recurrent seizures support a diagnosis of epilepsy. In patients with epilepsy, similar triggers, particularly alcohol ingestion and sleep deprivation (as in this patient), can precipitate a seizure or a more serious seizure. However, these seizures are not considered “provoked”; this term is reserved for isolated events in patients without epilepsy.

Distinguishing between focal and generalized epilepsy syndromes may not be possible if a patient has convulsions only. This patient's seizure was preceded by an aura, which is associated with

focal epilepsy. The age of onset in this patient (between 30 and 40 years) is also atypical for generalized epilepsy, which usually begins in adolescence or early adulthood.

A posttraumatic seizure can occur within a week of significant head trauma. This patient had head trauma without loss of consciousness 1 month before onset of her first recognized seizure. Her mild head trauma most likely is not related to her convulsive seizure or the diagnosis of epilepsy, particularly because her auras began before she hit her head.

uestion 7

A 48-year-old man is evaluated for increasing depression and suicidal ideation. He reports experiencing feelings of hopelessness, lack of initiative, and general disinterest over the past 5 years that recently have worsened and are now accompanied by mood swings, irritability, impatience, verbal abuse, and physical aggression. Thoughts of death and suicide often have been present in the past month. His gait has become slow and shuffling, and his balance is increasingly impaired. His wife says he is more forgetful than ever and unable to perform home repairs that he previously accomplished easily. He has had no hallucinations or delusions. The patient is retired from a 13-year career playing professional football. Other than minor football injuries, he has no significant medical history and has an unremarkable family history, including no neurologic and psychological disorders. The patient takes no medication.

On physical examination, vital signs are normal. Neurologic examination shows slow processing speed, mild dysarthria, slowed rapid alternating movements bilaterally, and a wide-based gait with decreased foot-floor clearance. The patient scores 20/30 on the Montreal Cognitive Assessment, losing points in the visuospatial/executive function, attention, orientation, and delayed recall sections.

Which of th e following is the most likely diagnosis?

A
Chronic traumatic encephalopathy

B
Dementia with Lewy bodies

C
Depression-related cognitive impairment

D
Parkinson disease

Answer & Critique

Correct Answer: A

Educational Objective: Diagnose chronic traumatic encephalopathy.

Key Point

Chronic traumatic encephalopathy is a progressive neurodegenerative disorder triggered by repetitive mild head injury as occurs in military combat veterans and athletes with a history of multiple concussions and subconcussions.

The most likely diagnosis for this patient is chronic traumatic encephalopathy. Chronic traumatic encephalopathy is a progressive neurodegenerative disorder triggered by repetitive mild head injury that has most often been described in military combat veterans and athletes with a history of multiple concussions and subconcussions. This patient's career as a professional football player would have made him particularly susceptible to this type of injury. Clinical symptoms typically manifest years or decades after repeated head trauma and present insidiously. Behavioral symptoms are common and include depression, suicidal ideation, apathy, and irritability. Disinhibition, impulsivity, and aggression can also occur in the later stages. Cognitive symptoms include problems with memory, attention, concentration, and executive function. With disease progression, poor judgment and poor insight become more prominent. Parkinsonism, disturbance of gait, and speech abnormalities often occur later in the disease course.

Although this patient exhibits mild parkinsonism on clinical examination, he lacks other features to support a diagnosis of dementia with Lewy bodies, such as fluctuating cognition, visual hallucinations, rapid eye movement sleep behavior disorder, and autonomic dysfunction. In addition, his age at symptom onset is unusual for dementia with Lewy bodies, which typically presents in the sixth decade of life or later.

Depression-related cognitive impairment refers to the cognitive deficits associated with depression and most often is characterized by frontal-subcortical dysfunction and slowed processing speed. Cognitive symptoms improve with treatment of depression. The patient has depression accompanied by suicidal ideation, but his history and constellation of additional neurologic and behavioral symptoms are more suggestive of chronic traumatic encephalopathy.

Parkinsonism tends to occur in chronic traumatic encephalopathy during the later stages of the disease. Comorbid neurodegenerative disease, such as Alzheimer disease, Lewy body disease, and Parkinson disease, can be seen in a percentage of patients with chronic traumatic encephalopathy at autopsy, and some evidence suggests that repetitive head injury is associated with increased risk of these disorders. This patient has slow and shuffling gait and bradykinesia but lacks the cardinal signs of idiopathic Parkinson disease, including resting tremor or rigidity, a unilateral onset, and asymmetric parkinsonism. The most likely diagnosis for his clinical syndrome of cognitive, behavioral, and motor decline is chronic traumatic encephalopathy.

Question 8

A 48-year-old woman is evaluated for a 12-month history of increasingly severe headaches. For the past 25 years, she has had monthly migraine without aura. The headaches have occurred one or two times per month, but over the past year, their severity has increased, with NSAIDs now providing only limited, temporary pain relief. Medications are ibuprofen and naproxen as needed (≤5 days/mo).

On physical examination, blood pressure is 116/70 mm Hg and pulse rate is 80/min. Other physical examination findings, including those from a neurologic examination, are normal.

An MRI of the brain shows several punctate hyperintensities in the bilateral subcortical white matter.

Which of the following is the most appropriate management?

A
Aspirin

B
Lumbar puncture

C
Magnetic resonance angiography

D
Rizatriptan

E
Timolol

Answer & Critique

Correct Answer: D

Educational Objective: Treat migraine in a patient with nonspecific MRI abnormalities.

Key Point

White matter signal abnormalities are typically seen on MRIs of patients with migraine, particularly in the posterior circulation and particularly in women; these lesions are benign and unrelated to neurologic examination abnormalities or cognitive anomalies

This patient should receive rizatriptan to treat migraine, which is no longer adequately controlled by NSAIDs. Other than increased intensity, the headache pattern has been stable for 25 years. Her history, physical examination findings, and MRI provide no evidence of a secondary headache disorder. The white matter signal abnormalities evident on the MRI are typical of those seen with migraine, specifically in the posterior circulation and particularly in women, as documented in several population-based studies. Data suggest that these lesions are benign and have no correlation with migraine frequency or the appearance of neurologic or cognitive anomalies or deficits. Initiation of a triptan is appropriate in patients with acute migraine who have not responded to treatment with one or more NSAIDs.

Aspirin is unlikely to relieve acute migraine pain that has not responded to two NSAIDs and would be unnecessary for secondary stroke prevention in this patient.

The patient has not reported any clinical events suggestive of stroke or a demyelinating disease, and her normal neurologic examination findings and the absence of any larger or periventricular white matter lesions on MRI would be unusual in multiple sclerosis. Lumbar puncture is thus not warranted in this patient.

Magnetic resonance angiography is also unnecessary. Although migraine is a contributor to stroke risk in women, this patient has no features suggestive of cerebral ischemia and has no aura or other risk factors for cerebrovascular disease.

Timolol is a migraine prophylactic drug that is effective in reducing the frequency of migraine attacks. Pharmacologic prophylaxis of migraine is indicated for headache frequency greater than 2 days per week (or 8 days per month) or use of acute medications, successfully or unsuccessfully, more than 2 days per week. Migraine frequency in this patient is too low to warrant introduction of daily migraine preventive medication.

Question 9

A 26-year-old woman is evaluated for a 10-year history of recurrent episodes of acute-onset feelings of fear and anxiety. These episodes initially occurred approximately four times per year but for the past 3 months have been occurring once or twice per month, especially when she is under stress. She describes the episodes as paroxysmal attacks of fear and anxiety associated with a dry mouth and a consistent "roller coaster" sensation in her stomach that typically last 15 seconds to 1 minute. With more intense attacks, she becomes momentarily confused; her boyfriend says she seems "fidgety" when this occurs. She feels well between episodes. Medical history is otherwise negative, and she takes no medication.

On physical examination, vital signs are normal. All other findings from the general physical and neurologic examinations are unremarkable.

A brain MRI and electroencephalogram are normal.

Which of the following is the most likely diagnosis?

A
Frontal lobe epilepsy

B
Juvenile absence epilepsy

C
Panic disorder

D
Psychogenic nonepileptic seizures

E
Temporal lobe epilepsy

Answer & Critique

Correct Answer: E

Educational Objective: Diagnose temporal lobe epilepsy.

Key Point

A rising epigastric sensation is the most common epileptic aura that originates in the temporal lobe; electroencephalographic and MRI findings are often normal.

This patient most likely has temporal lobe epilepsy. The rising epigastric sensation she describes is the most common epileptic aura that originates in the temporal lobe. Brief episodic anxiety with or without autonomic symptoms, such as dry mouth, also is characteristic of a temporal lobe seizure. These symptoms can occur independently or together (as in this patient) but are typically stereotyped in a given patient. The aura is a simple partial seizure, which can become a complex partial seizure and lead to altered sensorium and automatisms (such as “fidgety” behavior). The absence of focal findings on MRI and electroencephalography (EEG) does not rule-out a diagnosis of epilepsy and is in fact a common finding in temporal lobe epilepsy.

Frontal lobe epilepsy can present with different types of seizures, but a fearful and epigastric aura is not typical. Classically, frontal lobe seizures cause motor manifestations (focal jerking, bicycling movements) that awaken patients from sleep.

Juvenile absence epilepsy is a form of generalized epilepsy beginning at or after puberty that is characterized by absence seizures with or without convulsive seizures. An absence seizure is a brief loss of awareness, typically lasting 3 to 10 seconds. This type of seizure is not preceded by an aura.

Temporal lobe epilepsy is often misdiagnosed as panic disorder, which has some similar features. However, this patient's events are stereotyped and short in duration, characteristics that are more associated with temporal lobe seizures than panic attacks.

Although psychogenic nonepileptic seizures (PNES) can have numerous manifestations and should be part of the differential diagnosis, they are not the most likely cause of this patient's symptoms. PNES are less likely than epileptic seizures to be consistently stereotyped and brief in

duration. The fact that episodes can be triggered by stress does not necessarily distinguish between epileptic and nonepileptic seizures. Given the characteristic and consistent features of this patient's events, she should be treated for presumed epilepsy. If the patient does not respond to treatment, inpatient video EEG monitoring should be considered to make a definitive diagnosis.

Question 10

A 51-year-old woman is evaluated in the emergency department for sudden-onset severe headache and right-sided weakness followed by temporary loss of consciousness that occurred 30 minutes ago. According to her husband, she has hypertension treated with amlodipine and a 20-pack-year smoking history; she stopped smoking 12 years ago.

On physical examination, blood pressure is 158/68 mm Hg, pulse rate is 68/min and regular, and respiration rate is 10/min. Funduscopic examination findings are normal. Nuchal rigidity is noted. On neurologic examination, the patient does not follow commands and has flexor posturing to painful stimuli; pupils are reactive and symmetric in size and shape.

An electrocardiogram shows normal sinus rhythm and no ischemic changes.

Which of the following is the most appropriate next diagnostic test?

A
Catheter-based cerebral angiography

B
CT of the head without contrast

C
Lumbar puncture

D
MRI of the brain without contrast

Answer & Critique

Correct Answer: B

Educational Objective: Obtain CT without contrast in a patient with acute stroke.

Key Point

CT of the head without contrast is the most appropriate diagnostic test in a patient with acute stroke.

CT of the head without contrast is the most appropriate diagnostic test in this patient. She had sudden-onset severe headache followed by impaired consciousness, symptoms that are most concerning for hemorrhagic stroke caused by an aneurysmal subarachnoid hemorrhage or intracerebral hemorrhage. A neurologic examination by itself lacks sufficient predictive value to evaluate the source of impaired consciousness. Rapid imaging is required to initiate rapid treatment. CT of the head is readily available, can be performed quickly, and is the test of choice to rule out intracerebral hemorrhage, subarachnoid bleeding, and hydrocephalus, all of which may necessitate rapid neurosurgical intervention.

Catheter-based angiography is ultimately indicated in most patients with subarachnoid hemorrhage to determine the source of bleeding. However, CT of the head without contrast, which allows for more rapid imaging, should be performed first to evaluate for any condition (such as hydrocephalus from increased intracranial pressure) that can be rapidly reversed with emergency neurosurgical treatment.

Lumbar puncture should not be performed in a patient with stroke symptoms until the presence of a mass lesion has been excluded. If the patient has elevated intracranial pressure from mass effect, particularly in the cerebellum, lumbar puncture may worsen any cerebral herniation.

In the evaluation of a patient with symptoms of a stroke, MRI is time consuming, not readily available, and not cost-effective; this test also leaves the patient in a less monitored setting during the scanning than does CT. In the acute setting, stroke that requires rapid neurosurgical intervention should be diagnosed as quickly as possible.

Question 11

A 45-year-old man is evaluated for generalized weakness and stiffness. He has had slowly progressive weakness of the lower extremities for the past 5 years. The patient reports that he feels “wobbly” during ambulation, easily becomes fatigued, has bouts of stiffness in the upper and lower extremities, has occasional difficulty holding his hand above his head, and cannot easily stand up from a chair. He has had no diplopia, numbness, or tingling. He says that sometimes it is difficult to release his grip after turning a door knob. Medical history includes cardiomyopathy, first-degree heart block, and cataract surgery 1 year ago. He has a brother with muscle weakness. His only medication is metoprolol.

On physical examination, vital signs are normal. Bilateral ptosis that does not worsen with sustained upward gaze is noted, as is bilateral facial drooping. Speech is dysarthric. Proximal limb muscles are tight, and finger abductors and foot dorsal flexors are weak bilaterally. A delay in releasing his hand grip and slow relaxation of the muscles after percussion are noted. Gait is stiff and unstable.

Which of the following is the most likely diagnosis?

A
Becker muscular dystrophy

B
Inclusion body myositis

C
Lambert-Eaton myasthenic syndrome

D
Myasthenia gravis

E
Myotonic dystrophy

Answer & Critique

Correct Answer: E

Educational Objective: Diagnose myotonic dystrophy.

Key Point

Myotonic dystrophy should be considered in all patients with weakness, fatigue, and a myopathic waddling gait who also have muscle stiffness and delayed grip relaxation.

This patient most likely has myotonic dystrophy. Whereas muscle weakness and fatigue are present in a wide range of myopathies, neuromuscular junction disorders, and other conditions, the presence of myotonia—an impairment of muscle relaxation secondary to increased cellular membrane hyperexcitability—narrows the differential diagnosis. Myotonic dystrophy is the most common myotonic disorder, with accompanying symptoms of cataract, cardiomyopathy, cardiac conduction abnormalities, diabetes mellitus, and alopecia. This condition should be considered in all patients with weakness, fatigue, and a myopathic waddling gait who also have muscle stiffness and delayed grip relaxation. The diagnosis should be confirmed by electromyography; confirmatory genetic testing (for myotonic dystrophy type 1) is available commercially. Myotonic dystrophy type 1 is more common and preferentially involves distal limb and facial muscles, whereas the less common type 2 preferentially affects proximal muscles. An increased awareness of comorbidities of myotonic dystrophy and aggressive management of its cardiac complications, which can increase mortality, are recommended.

Becker muscular dystrophy typically starts in childhood, but its progression can be variable. Its pattern of weakness is predominantly proximal, and calf hypertrophy is present; myotonia is not.

Inclusion body myositis is a slowly progressive inflammatory myopathy that predominantly affects distal upper extremity flexors and quadriceps. Asymmetric involvement is common, but myotonia is not a feature.

Although fatigue and weakness can occur in Lambert-Eaton myasthenic syndrome and myasthenia gravis, neither of these conditions is associated with myotonia.

Question 12

A 67-year-old man is evaluated in the emergency department for sudden onset of severe headache that has not abated over the past 24 hours.

On physical examination, temperature is 37.4 °C (99.3 °F), blood pressure is 168/78 mm Hg, pulse rate is 68/min and regular, and respiration rate is 12/min. Nuchal rigidity is noted. The left pupil is 5 mm in diameter and unreactive to light, and the right pupil is 3 mm in diameter and reactive to light. A neurologic examination shows normal mental status and motor function.

A CT of the head without contrast is normal.

Which of the following is the most appropriate next diagnostic test?

A
Lumbar puncture

B
Magnetic resonance angiography of the brain

C
Magnetic resonance venography of the brain

D
MRI of the brain

Answer & Critique

Correct Answer: A

Educational Objective: Diagnose a subarachnoid hemorrhage with lumbar puncture.

Key Point

When the suspicion of a subarachnoid hemorrhage is high and the noncontrast CT scan of the head is normal, a lumbar puncture is required to evaluate the cerebrospinal fluid for erythrocytes or xanthochromia.

This patient should undergo lumbar puncture. He reports sudden onset of a severe headache, most likely a thunderclap headache. Thunderclap headache is defined as a severe headache that reaches maximum intensity within 60 seconds of onset. Although classically associated with subarachnoid hemorrhage (SAH), thunderclap headache also may be caused by other conditions, ranging from benign to life-threatening ones. Because approximately 25% of thunderclap headache presentations result from an SAH, this type of headache should be approached as a neurologic emergency. Although other causes are possible, including dural sinus thrombosis, meningitis, and migraine, the presence of a dilated unreactive pupil suggests external compression of the left oculomotor nerve (cranial nerve III). In the presence of a normal mental status, cerebral herniation and increased intracranial pressure are unlikely, but an aneurysm of the left posterior communicating artery is possible that may not be visible on a noncontrast CT scan of the head. Patients with an aneurysmal SAH may first experience less extensive bleeding that also is not visible on a noncontrast head CT before more significant bleeding occurs. After this initial or “sentinel” bleeding, the patient is at high risk for a clinically significant SAH with associated high morbidity and mortality. Therefore, establishing the diagnosis is a priority.

When the suspicion of an SAH is high and the noncontrast CT scan of the head is normal, a lumbar puncture is required to evaluate the cerebrospinal fluid (CSF) for erythrocytes or xanthochromia. Xanthochromia describes a yellow discoloration of the CSF from breakdown of erythrocytes, which may not develop for at least 6 hours after the initial event.

Magnetic resonance angiography (MRA) is premature before SAH is excluded. Once SAH has been ruled out, MRA may be needed to exclude other arterial causes, such as cervicocephalic

arterial dissection. Internal carotid artery dissection can cause pupillary abnormalities, but these are typically from a Horner syndrome, with a smaller pupillary diameter in the affected eye.

Similarly, magnetic resonance venography (MRV) of the brain should not be performed until SAH is excluded. MRV is used to diagnose deep venous thrombosis and cerebral venous sinus thrombosis. Although the latter disorder sometimes presents with thunderclap headache, it is unlikely to cause a dilated unreactive left pupil.

The usefulness of MRI for diagnosing SAH remains under investigation. MRI may ultimately be required if the CSF is normal to rule out other disorders.

Question 13

A 69-year-old man is evaluated for a 1-year history of increasing word-finding difficulties. The patient also reports occasional difficulty recalling names of objects and people and has had problems comprehending conversations. His daughter reports sometimes not understanding what her father is saying because of his frequent use of filler words, such as “that thing” and “you know”; she says that otherwise his mind seems sharp, his cognition unimpaired, and his memory excellent. He has no other significant medical history, and he takes no medication. His older brother had onset of dementia at age 56 years, and his father developed dementia at age 60 years.

On physical examination, vital signs are normal. General physical examination results are unremarkable, and a neurologic examination yields no focal findings. However, the patient has trouble answering even simple questions about where he lives or what he had for breakfast and is unable to name simple objects.

Results of laboratory studies, including a complete blood count, comprehensive metabolic profile, and thyroid function studies, are normal.

An MRI of the brain is normal.

Which of the following is the most appropriate next step in management?

A
Determination of apolipoprotein E (*APOE ε4*) status

B
Observation with reevaluation in 3 to 6 months

C
Speech and language therapy

D
Trial of donepezil

Answer & Critique

Correct Answer: C

Educational Objective: Treat primary progressive aphasia.

Key Point

In primary progressive aphasia, occupational therapy for speech and language can teach the patient and family compensatory strategies to improve communication.

This patient should have speech and language therapy. His history is concerning for the initial stages of primary progressive aphasia, which is characterized by the progressive loss of language function with relative sparing of other cognitive domains early in the course of the disease. Primary progressive aphasia is most commonly associated with frontotemporal dementia but also may be a manifestation of Alzheimer disease. Different clinical subtypes of primary progressive aphasia exist that are based on the pattern of language impairment, but each progresses insidiously and eventually results in significant disturbance of communication. The disorder results in significant disability but can be very difficult to diagnose early in its course. Occupational therapy for speech and language can teach the patient and family compensatory strategies to improve communication. This treatment is most beneficial early in the disease when motivation, insight, and learning capabilities are greatest.

Determination of the patient's apolipoprotein E (*APOE ?4*) status could help define his risk for developing Alzheimer disease but would not confirm if he has this disorder. Additionally, the information obtained by assessing his genotype would not be informative if the underlying cause is frontotemporal dementia.

Observation with reevaluation in 3 to 6 months is not the most appropriate next step in management because it would delay intervention that could diminish early symptoms.

Donepezil, a cholinesterase inhibitor, is not FDA approved for the treatment of primary progressive aphasia or frontotemporal dementia. For primary progressive aphasia that is due to underlying Alzheimer disease, standard medications approved by the FDA for Alzheimer disease may be

appropriate for symptomatic benefit. However, the first step in management should be occupational therapy for speech and language, especially before a diagnosis of Alzheimer disease is established.

Question 14

A 72-year-old woman is evaluated for a 6-month history of gradually worsening, nonsuppressible involuntary movements. The patient first noticed twitching movements of the lower part of the face, with occasional unintended thrusting of the tongue through the lips and biting of the cheeks inside the mouth. She further reports pressure and a pulling sensation at the back of the neck that causes her head to pull backward suddenly and the occasional tendency to drop objects from her hands secondary to uncontrollable jerking movements. The patient has chronic gastroparesis that is treated with metoclopramide and bipolar disorder that is well controlled with lamotrigine and quetiapine. She has no family history of a movement disorder or any neurologic disease.

On physical examination, temperature is 37.5 °C (99.5 °F), blood pressure is 145/76 mm Hg, and pulse rate is 80/min. Frequent stereotyped pursing movements of the lips, occasional tongue protrusion and forceful jaw closure, continual slow and nonrhythmic movements of the fingers, and recurrent cervical retrocollis are noted. Occasional rapid jerking movements of the arms and infrequent facial grimacing also are present. Gait is slow and marked by short steps and reduced arm swing.

Which of the following is the most appropriate next step in management?

A
Change quetiapine to risperidone

B
Discontinue metoclopramide

C
Start carbidopa-levodopa

D
Start tetrabenazine

Answer & Critique

Correct Answer: B

Educational Objective: Treat drug-induced tardive dyskinesia.

Key Point

The most appropriate treatment of medication-related tardive dyskinesia is discontinuation of the causative dopamine blocker agent.

The most appropriate next step is to discontinue the dopamine receptor antagonist metoclopramide. This patient has prominent craniofacial features of chorea and dystonia that are characteristic of tardive dyskinesia. She most likely has medication-related dyskinesia, and discontinuation of the causative dopamine blocker agent is required. Physicians prescribing chronic dopamine blocker antinausea agents should warn their patients about the risk of tardive dyskinesia, a complication that can lead to long-lasting or permanent involuntary movements. Old age and female sex increase the risk of this complication.

Typical and most atypical antipsychotic agents can cause tardive dyskinesia. The main exceptions are quetiapine and clozapine. Because atypical antipsychotic agents also increase the risk of symptoms of tardive dyskinesia becoming permanent, risperidone should be avoided in this patient unless absolutely indicated

Carbidopa-levodopa is appropriate treatment of Parkinson disease, and this patient's slow and narrow-based gait is typical of parkinsonism. However, carbidopa-levodopa can aggravate dyskinetic movements and thus should be avoided in this patient.

Tetrabenazine, a dopamine depleter, has been approved by the FDA for treatment of chorea in Huntington disease. Several studies also have shown its efficacy in reducing tardive dyskinesia, but this remains an off-label use. Because tardive dyskinesia often spontaneously resolves within several months of removal of the causative agent, the immediate use of tetrabenazine in this patient with a mood disorder is unjustified, especially in light of the drug's serious mood-related complications.

Question 15

A 40-year-old woman is seen for a follow-up evaluation of multiple sclerosis, which was diagnosed 1 month ago. The patient reports feeling generally well. She has no significant medical history and does not drink or smoke. Her only medication is interferon beta-1a, which she has been taking since diagnosis and tolerates well.

On physical examination, vital signs are normal. Neurologic examination reveals internuclear ophthalmoplegia, right arm weakness, and mild ataxia, which were present at diagnosis and have remained stable. All other physical examination findings are unremarkable.

Which of the following is indicated for periodic monitoring of this patient's disease -modifying therapy?

A
JC virus antibody measurement

B
Ophthalmologic evaluation

C
Serum aminotransferase measurement

D
Serum amylase and lipase measurement

Answer & Critique

Correct Answer: C

Educational Objective: Monitor patients for adverse effects of multiple sclerosis therapies.

Key Point

In patients taking an interferon beta as a disease-modifying therapy for multiple sclerosis, serum aminotransferase levels should be measured every 3 to 6 months to monitor for autoimmune hepatitis.

This patient being treated with an interferon beta preparation should have her serum aminotransferase levels measured every 3 to 6 months. Interferon injections are associated with rare autoimmune hepatitis. Therefore, monitoring of liver status by periodic measurement of serum aminotransferase levels is appropriate in patients with multiple sclerosis (MS) who take an interferon beta preparation as a disease-modifying therapy. Although the optimal frequency of monitoring has not been established, most cases of severe hepatotoxicity appear to occur early in therapy. It is also recommended that concurrent use of potentially hepatotoxic agents, such as alcohol, be avoided while taking interferon therapy. Other more common adverse effects include injection site reactions, flu-like symptoms, and depression.

JC virus antibody screening is currently recommended as a risk mitigation strategy for patients with MS treated with natalizumab because elevated levels of JC virus antibody have been correlated with an increased risk of progressive multifocal leukoencephalopathy (PML) in patients taking this drug. However, no incidences of PML have been reported in patients (such as this one) treated with interferon beta injections. Therefore, monitoring for JC virus antibody is not indicated.

Frequent ophthalmologic examinations are recommended for patients taking fingolimod for MS because of the risk of macular edema. No specific ocular risks are associated with interferon injections.

Teriflunomide has been associated with pancreatitis, and monitoring of the serum amylase and lipase levels is indicated for patients with MS who take this medication. Interferon beta preparations have not been associated with this adverse effect.

Question 16

A 68-year-old woman is evaluated 1 month after having an ischemic stroke of the left thalamus. She now has only residual right-sided anesthesia. The patient has hypertension and dyslipidemia, both well controlled by medication, and had been taking a daily aspirin before the stroke. Medications are lisinopril, chlorthalidone, aspirin, and rosuvastatin.

On physical examination, blood pressure is 128/68 mm Hg and pulse rate is 68/min and regular. Findings from the remainder of the general physical examination are normal, including no carotid bruits on cardiac examination. Neurologic examination findings include decreased sensation to light touch and pinprick throughout the right side.

Which of the following is the most appropriate treatment?

A
Add clopidogrel

B
Add dipyridamole

C
Substitute ticlopidine for aspirin

D
Substitute warfarin for aspirin

Answer & Critique

Correct Answer: B

Educational Objective: Treat with antiplatelet agents for secondary stroke prevention.

Key Point

The combination of aspirin and dipyridamole has been shown to be superior to aspirin alone in reducing the risk of recurrent stroke.

Dipyridamole should be added to this patient's medication regimen. She had a small subcortical infarction despite taking daily aspirin before the stroke. The combination of aspirin and dipyridamole has been shown to be superior to aspirin alone in reducing the risk of recurrent stroke.

The combination of aspirin and clopidogrel versus aspirin alone in patients with small subcortical infarcts (lacunes) was associated with increased mortality without the benefit of reducing the risk of recurrent stroke in the Secondary Prevention of Small Subcortical Strokes (SPS3) trial. Similarly, in the Management of Atherothrombosis with Clopidogrel in High-Risk Patients with Recent Transient Ischemic Attacks or Ischemic Stroke (MATCH) trial, the combination of dual antiplatelet agents was associated with an increased risk of hemorrhagic complications that offset any potential clinical benefit. The combination of aspirin and clopidogrel thus has limited utility in the secondary prevention of stroke.

Ticlopidine is not first-line treatment for secondary stroke prevention. Although superior to aspirin in preventing a second stroke, ticlopidine is associated with the serious adverse effects of agranulocytosis and thrombotic thrombocytopenic purpura and thus is considered a second-line agent.

Warfarin should not be substituted for aspirin because no evidence of atrial fibrillation or other high-risk cardioembolic sources of stroke was detected in this patient.

Question 17

A 27-year-old woman comes to the office to discuss medications 3 days after experiencing a first seizure. MRI evaluation on the day of the seizure showed left mesial temporal sclerosis, and a subsequent electroencephalogram was significant for temporal sharp waves, findings consistent with temporal lobe epilepsy. She has polycystic ovary syndrome and requires a daily estrogen-progestin combination for symptom management and contraception.

Physical examination findings, including vital signs, are normal.

Which of the following antiepileptic drugs is most appropriate?

A
Carbamazepine

B
Lamotrigine

C
Levetiracetam

D
Oxcarbazepine

E
Topiramate

Answer & Critique

Correct Answer: C

Educational Objective: Treat epilepsy in a woman taking oral contraceptives.

Key Point

Levetiracetam has no major drug-to-drug interactions with hormonal contraceptives and thus is appropriate to use in women with epilepsy who take oral contraceptives.

This patient's epilepsy, which is strongly suggested by her MRI and electroencephalographic findings, should be treated with an antiepileptic drug (AED). Of the AEDs listed, levetiracetam is most appropriate for a woman who takes oral contraceptive pills for polycystic ovary syndrome (PCOS) and also relies on them for contraception because it has no significant interactions with synthetic hormones. Most AEDs, particularly older agents, induce hepatic enzymes that alter the metabolism of hormonal contraceptives. This alteration may lead to unpredictable levels of synthetic estrogens and progestin; additionally, when the contraceptives are used to prevent pregnancy, increased failure can occur in women taking AEDs.

Carbamazepine and oxcarbazepine induce cytochrome CYP3A4 and thus affect the metabolism of synthetic estrogens and progestins, which makes many forms of hormonal contraception ineffective. Neither drug is an appropriate treatment for this patient. An intrauterine device (IUD) is the preferred method of contraception for women taking enzyme-inducing AEDs, but an IUD would not address this patient's PCOS symptoms.

Lamotrigine has unique interactions with hormonal contraceptives. Synthetic estrogens induce the clearance of lamotrigine by as much as 50%, which means that higher dosages of lamotrigine have to be administered to patients taking an oral contraceptive and that AED levels will increase during the placebo week of contraceptive therapy. If needed, lamotrigine can be administered with extended-cycle oral contraceptives, but an IUD is the preferred method of contraception for patients taking lamotrigine. Lamotrigine also decreases levels of synthetic progestins by 20%, although the clinical significance of this decrease is unknown.

Topiramate also increases clearance of synthetic estrogens. Although the clinical significance of this effect with lower doses of topiramate is debated, the World Health Organization advises against combining oral contraceptives with any dose of topiramate and recommends an IUD for contraception in patients taking this drug. Furthermore, topiramate is considered a class D drug for pregnancy because of the increased risk of facial clefting in exposed children, Therefore, it should not be used as a first-line agent in women of childbearing age.

Question 18

An 83-year-old woman is evaluated in the emergency department for a 36-hour history of left-sided weakness. She has noticed no changes in vision or speech. The patient has hypertension and dyslipidemia. Medications are aspirin, losartan, metoprolol, and atorvastatin.

On physical examination, blood pressure is 168/102 mm Hg, pulse rate is 78/min and regular, and respiration rate is 16/min. Other findings from the general medical examination are normal. Neurologic examination shows grade 4/5 weakness of the left face, arm, and leg; dysarthria; and unsteady gait. Her score on the National Institutes of Health Stroke Scale is 8, indicating a moderate stroke; she coughed after attempting to swallow 30 mL of water.

Results of laboratory studies are normal.

An electrocardiogram is normal. A CT scan of the head without contrast shows an infarct in the right pons.

Which of the following is most likely to r educe the 1-year mortality risk in this patient?

A
Add clopidogrel

B
Administer labetalol intravenously

C
Administer recombinant tissue plasminogen activator (rtPA)

D
Admit to the stroke unit

Answer & Critique

Correct Answer: D

Educational Objective: Treat stroke with admission to the stroke unit.

Key Point

In patients with newly diagnosed stroke, admission to an organized inpatient stroke unit compared with a general medical ward is associated with a reduction in mortality at 1 year, with benefits persisting up to several years after stroke.

This patient has had an acute ischemic stroke and should be admitted to the inpatient stroke unit. Several studies have shown that admission of patients with stroke to an organized inpatient stroke unit compared with a general medical ward is associated with a reduction in mortality at 1 year, with benefits persisting up to several years after stroke. Stroke units are beneficial because of the multidisciplinary nature of care, with an emphasis on specialized nursing, early mobilization, removal of urinary bladder catheters, and adherence to stroke-specific protocols. An important component of the success of stroke units is early referral for rehabilitation services to promote stroke recovery.

Adding clopidogrel to this patient's medication regimen is inappropriate management because the combination of aspirin and clopidogrel has not been shown to be effective and may increase the risk of hemorrhage over the next 3 months. The combination of aspirin and clopidogrel recently was found to reduce the risk of recurrent stroke compared with aspirin alone when administered within 24 hours of transient ischemic attack or minor stroke (National Institutes of Health [NIH] Stroke Scale score less than 5). Because this patient is beyond the 24-hour mark and scored 8 on the NIH Stroke Scale, no evidence supports giving her combination therapy.

This patient's blood pressure is within the acceptable range for someone who has had an acute ischemic stroke. Immediate blood pressure lowering with labetalol or other antihypertensive agents in patients who do not receive intravenous thrombolysis is only recommended if the blood pressure is greater than 220/120 mm Hg or if a high risk or evidence of other end-organ damage exists; neither situation applies.

This patient is well beyond the acceptable timeframe for thrombolysis (3 hours).

Question 19

A 24-year-old man is seen for management of seizures. His first seizure occurred 5 years ago, at which time he had a normal MRI and electroencephalogram. Since that time, he has had two additional seizures, one 2 years ago and the other last week. All seizures have been convulsive and occurred without warning. The patient reports being under stress or sleep deprived around the time of the seizures. He has had no paroxysmal symptoms, including staring spells or morning jerks. He takes no medication.

Physical examination findings, including vital signs, are unremarkable.

Laboratory studies, including a complete blood count, a comprehensive metabolic profile, and measurement of serum thyroid-stimulating hormone level, have normal results.

Which of the following treatments is most appropriate?

A
Carbamazepine

B
Gabapentin

C
Phenytoin

D
Topiramate

Answer & Critique

Correct Answer: D

Educational Objective: Treat generalized epilepsy.

Key Point

Topiramate is a broad-spectrum antiepileptic drug that is appropriate for treating both focal and generalized epilepsy, especially when the specific epilepsy syndrome is unknown.

This patient should be treated with a broad-spectrum antiepileptic drug (AED), such as topiramate. Given his history of recurrent unprovoked seizures, he clearly has an epilepsy syndrome, but the seizure features and results of ancillary testing do not definitively identify what kind of epilepsy syndrome. When it is unclear if a patient has focal or generalized epilepsy, treatment should be a broad-spectrum AED that can be used to treat both generalized and partial epilepsy syndromes. Topiramate is a broad-spectrum agent appropriate for both focal and generalized epilepsy; other appropriate drugs are lamotrigine, levetiracetam, valproic acid, and zonisamide. Patients starting topiramate should be counseled about the risk of developing kidney stones and the need to stay hydrated. Topiramate may offer additional advantages to patients with comorbid headaches. It also is associated with weight loss and thus may be of added benefit in patients who are overweight. However, the drug may have cognitive adverse effects, such as word-finding difficulty, in some patients. The risk of rash and Stevens-Johnson syndrome should be discussed with all patients starting an AED.

Carbamazepine, gabapentin, and phenytoin are all narrow-spectrum AEDs used to treat partial-onset epilepsies. They have the potential to exacerbate generalized epilepsy and may provoke absence status epilepticus. They should be used when the seizure characteristics or MRI and electroencephalogram clearly support the diagnosis of a partial onset seizure. Typical features suggestive of partial onset include specific auras (déjà vu or a rising epigastric sensation) and unilateral clonic shaking before onset.

Question 20

A 72-year-old man is evaluated for a 1-year history of progressively impaired gait and balance. He reports that he walks more slowly and is not as agile as he used to be, attributing a recently increased number of falls to not paying enough attention before tripping. In the past 6 months, he has had occasional problems recalling details of recent conversations and events, completing tasks around the house in a timely manner, and organizing and balancing his checkbook despite having been an accountant before retiring. The patient also reports some urinary urgency and frequency but otherwise feels well. He has hypertension treated with hydrochlorothiazide and no history of traumatic brain injury, meningitis, or intracranial hemorrhage.

On physical examination, vital signs are normal. General medical examination findings are unremarkable. On neurologic examination, gait is slow, with poor foot clearance, shuffling, multistep turns, and intermittent hesitation. Tandem gait is impaired. The remainder of the physical examination is unremarkable. He scores 23/30 on the Mini–Mental State Examination, with points deducted on the delayed recall and serial 7 calculation sections.

An MRI of the brain is shown.

Which of the following is the most appropriate next step in management?

A

Brain magnetic resonance angiography

B

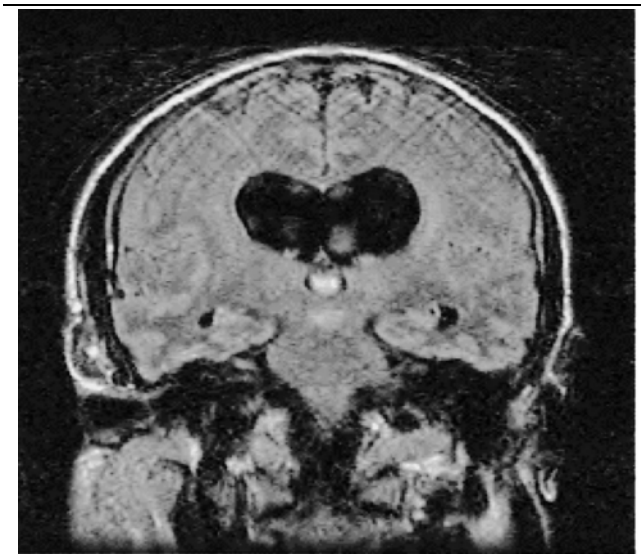
Large-volume lumbar puncture

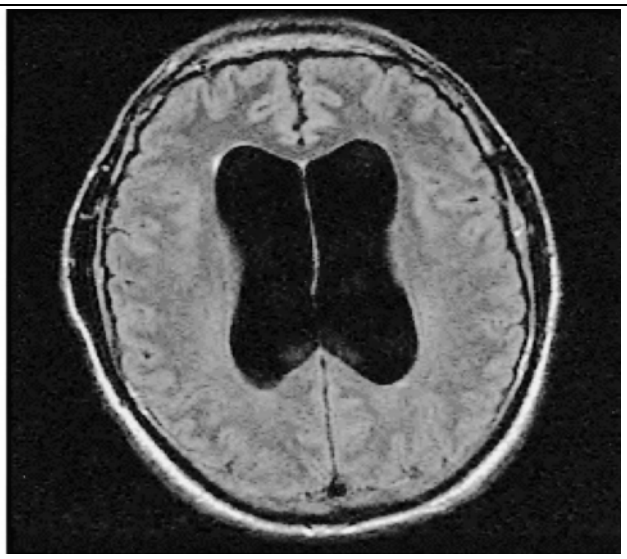
C

Trial of donepezil

D

Trial of levodopa





Answer & Critique

Correct Answer: B

Educational Objective: Diagnose normal pressure hydrocephalus.

Key Point

Large-volume lumbar puncture should be performed before placement of a ventriculoperitoneal shunt in patients with normal pressure hydrocephalus.

Large-volume lumbar puncture is indicated in this patient with likely normal pressure hydrocephalus (NPH). NPH is the most likely diagnosis in the setting of the triad of gait abnormalities, cognitive impairment, and urinary disturbance, especially when neuroimaging studies show enlarged ventricles out of proportion to cortical atrophy. NPH is a potentially reversible cause of cognitive and motor decline. A large-volume lumbar puncture with measurement of intracranial pressure and removal of 30 to 50 mL of cerebrospinal fluid (CSF) should be performed before consideration of placement of a ventriculoperitoneal shunt. Cognitive, balance, and gait examinations before and after the lumbar puncture can be useful to evaluate for potential response to shunting. If a positive response to the initial lumbar puncture is not seen and the clinical suspicion remains high, serial lumbar punctures or continuous lumbar drainage can be considered.

Periventricular white matter changes can be seen on the brain MRI and may have an identical appearance to what is seen in small-vessel vascular disease. However, without additional clinical or neuroradiologic evidence of a previous infarction, extensive evaluation with neurovascular

imaging to assess for a cause of these radiologic changes on brain MRI is not warranted. Periventricular hyperintensities are a frequent finding in normal pressure hydrocephalus and are thought to be related to transependymal resorption of CSF.

The cholinesterase inhibitor donepezil is sometimes effective in improving cognitive symptoms and function in patients with Alzheimer disease but has no benefit for the gait and cognitive disturbances typical of normal pressure hydrocephalus.

Although this patient has evidence of lower-body parkinsonism, he lacks other findings that suggest the presence of idiopathic Parkinson disease, such as a resting tremor, asymmetric onset of motor symptoms, and typical nonmotor symptoms. Therefore, levodopa is not likely to result in any symptomatic benefit.

Question 21

A 40-year-old man is evaluated in the emergency department for a headache that started 1 day ago while he was lifting weights. He first experienced a severe, sharp, right periorbital pain associated with nausea and ipsilateral neck pain. Although the pain has lessened in intensity, it has persisted, and this morning he had an episode of right monocular visual loss resolving spontaneously after several minutes. The patient has a history of monthly migraine without aura that typically lasts 6 hours and is characterized by bilateral frontotemporal throbbing, pain associated with photophobia, and nausea. He says that his current headache pain is “different” from the pain he experiences during migraine episodes and that the neck pain is new. His only medication is naproxen as needed.

On physical examination, blood pressure is 130/86 mm Hg and pulse rate is 72/min. Palpation of the neck elicits pain. Right ptosis and miosis are noted, but all other physical examination findings are unremarkable.

A CT scan of the head shows normal findings.

Which of the following is the most likely diagnosis?

A
Carotid artery dissection

B
Cluster headache

C
Migraine

D
Vertebral artery dissection

Answer & Critique

Correct Answer: A

Educational Objective: Diagnose carotid artery dissection.

Key Point

Carotid artery dissection should be suspected in a patient with acute headache and neck pain associated with Horner syndrome.

The patient most likely has had a carotid artery dissection. Despite his migraine history, the report of a different type of headache should raise suspicion of a secondary headache. Cervicocephalic dissection is an uncommon but important cause of stroke, especially in persons younger than 50 years. The presence of ipsilateral neck pain and ischemic complications, such as transient monocular visual loss and Horner syndrome (miosis, ptosis, and anhidrosis), is characteristic of carotid artery dissection and may not be associated with preceding trauma. The cause of an associated stroke is primarily thrombus formation at the site of dissection with subsequent artery-to-artery embolism. The imaging modality of choice is an MRI of the soft tissues in the neck, which will demonstrate a crescent-shaped hematoma within the internal carotid artery wall on T1-weighted images. Aspirin is considered the treatment of choice to prevent ongoing ischemic complications or stroke.

Cluster headache is a primary headache disorder classified as a trigeminal autonomic cephalalgia. This type of headache presents with unilateral head pain, which is typically periorbital or temporal (“trigeminal”) but sometimes may affect the face or neck. Cranial autonomic features, such as ptosis, miosis, tearing, and nasal congestion, are characteristic. Cluster headaches appear in a repetitive fashion, one to eight times daily, and are brief, with durations between 15 minutes and 3 hours. Related trigeminal autonomic cephalgias, such as chronic paroxysmal hemicrania or short-lasting unilateral neuralgiform headaches with conjunctival injection and tearing (SUNCT syndrome), occur with greater frequency and are of shorter duration, lasting minutes and seconds respectively. In this patient, the headache developed abruptly and has lasted an entire day, with no prior pattern indicative of these disorders.

The patient has a history of migraine, but his description of a “different” headache should raise concerns for secondary explanations. The duration of the attack is not outside the acceptable

range for migraine (4 to 72 hours), and migraine can present with either unilateral or bilateral discomfort. Visual aura is described by 25% to 35% of those with established migraine, but monocular visual loss is much more uncommon than binocular hemifield impairment. Ptosis and miosis resulting from migraine are quite uncommon. Red flags in this patient's case include the “different” nature of the headache, the new symptoms of neck pain and monocular visual dysfunction, the abrupt onset of pain during physical exertion, and (most importantly) the abnormal physical examination findings. This combination renders migraine unlikely.

Vertebral artery dissection can present with acute head or neck pain associated with physical exertion or trauma but also can occur spontaneously. The most common symptom is headache, but neurologic symptoms or deficits also occur. As many as 25% of ischemic strokes in younger patients result from either carotid or vertebral artery dissection. Because the vertebrobasilar supply of the occipital cortex or cerebellum may be affected, symptoms of loss of vision or balance are common. Although ptosis and miosis may arise from infarction of the lateral medulla (Wallenberg syndrome) in vertebral dissection, they are always accompanied by other findings, such as vertigo, dysarthria, dysphagia, ataxia, and loss of pain and temperature sensation ipsilaterally in the face and contralaterally in the body.

Question 22

A 30-year-old man is evaluated in the hospital for hyponatremia and dizziness. He reports a 3-day history of fatigue, headache, and imbalance. The patient has had difficult-to-manage nonlesional epilepsy since age 9 years and has required multiple drugs to maintain a seizure rate of only two or three per month. He has no other significant medical history. Medications are oxcarbazepine, levetiracetam, topiramate, and clonazepam.

On physical examination, mental status is normal. Temperature is 37.3 °C (99.1 °F), blood pressure is 95/60 mm Hg, pulse rate is 100/min, and respiration rate is 14/min. Examination of the eyes reveals end-gaze nystagmus in both directions of gaze; the optic discs are sharp. Gait is ataxic.

Laboratory studies:

Creatinine	0.7 mg/dL (61.9 µmol/L)
Electrolytes	
Sodium	123 mEq/L (123 mmol/L)
Potassium	3.5 mEq/L (3.5 mmol/L)
Chloride	90 mEq/L (90 mmol/L)
Bicarbonate	23 mEq/L (23 mmol/L)

Which of the following medications is most likely responsible for this patient's findings?

A
Clonazepam

B
Levetiracetam

C
Oxcarbazepine

D
Topiramate

Answer & Critique

Correct Answer: C

Educational Objective: Diagnose oxcarbazepine-associated hyponatremia.

Key Point

Oxcarbazepine is associated with hyponatremia in 20% to 30% of the patients who take it; although symptoms are generally mild and not clinically significant, severe hyponatremia occurs in 8% to 12% of these patients.

Oxcarbazepine is the drug most likely to be responsible for this patient's symptoms and abnormal laboratory findings, and its dosage should be reduced. The drug is associated with hyponatremia in 20% to 30% of the patients taking this medication. In most patients, symptoms associated with hyponatremia are generally mild and not clinically significant. However, severe hyponatremia occurs in 8% to 12% of these patients. Higher doses of oxcarbazepine and polytherapy with other drugs increase the risk of hyponatremia. Although a direct effect on the kidneys has been proposed, the exact mechanism of oxcarbazepine-induced hyponatremia is not well understood. Decreasing the dosage or discontinuing oxcarbazepine, if safe to do so, can help correct hyponatremia. Either of these steps should be taken in conjunction with standard evaluation and management of hyponatremia, including free water restriction. Hyponatremia also can occur with carbamazepine but is much more common and severe with oxcarbazepine use.

This patient's dizziness, end-gaze nystagmus, and ataxia also are likely adverse effects of oxcarbazepine use, although they could be related to the hyponatremia itself. These symptoms and findings can be seen with all antiepileptic drugs (AEDs), particularly in polytherapy, but are most common with AEDs that act on sodium channels, including oxcarbazepine, carbamazepine, lamotrigine, and phenytoin.

Clonazepam, levetiracetam, and topiramate are not associated with hyponatremia. Clonazepam can cause sedation, tolerance, and dependence. The most common adverse effect of levetiracetam is irritability and other adverse effects on mood. Topiramate can cause a mild, usually subclinical acidosis and a low serum bicarbonate level but does not affect the serum

sodium level. It is also associated with kidney stones, weight loss, and acute angle-closure glaucoma.

Question 23

A 68-year-old woman is evaluated for memory deficits. She retired from her position as a high school principal 2 years ago. In the past 6 months, she has had increasing forgetfulness, difficulty organizing her belongings, and problems with concentration and indecisiveness; during this period, she also has noticed fatigue, decreased energy, difficulty falling asleep, diminished interest in reading, and decreased appetite, which has caused her to lose 4.5 kg (10.0 lb). The patient has remained independent in activities of daily living, although she has forgotten to pay several monthly bills. She moved closer to her son last year but now has few opportunities to see her friends, which has resulted in feelings of isolation and sadness. The patient had a depressive episode 28 years ago after her husband's death. She takes no medication.

On physical examination, vital signs and general physical examination findings are normal. Neurologic examination reveals psychomotor slowing without decremental response on repetitive finger tapping. The patient scores 27/30 on the Mini–Mental State Examination, losing three points in the attention and calculation section.

Results of a complete blood count, a comprehensive metabolic profile, thyroid function tests, and urinalysis are normal.

Which of the following is the most appropriate next step in management?

A
Carbidopa-levodopa

B
Donepezil

C
Sertraline

D
Clinical observation

Answer & Critique

Correct Answer: C

Educational Objective: Treat depression-related cognitive impairment.

Key Point

First-line treatment of major depression in patients with cognitive impairment is pharmacotherapy, with or without psychotherapy.

The patient's symptoms are consistent with a major depressive episode, which should be treated with sertraline. More than half of patients with late-life major depression exhibit clinically significant cognitive impairment, most frequently affecting processing speed, executive function, and visuospatial ability. Her feelings of isolation and sadness, previous depressive episode, loss of interest in reading, loss of energy, poor concentration, indecisiveness, and significant weight loss are all suggestive of major depression. Depression-related cognitive impairment, historically known as pseudodementia, can be difficult to distinguish from early degenerative diseases. Cognitive testing may show objective impairment of working memory, attention, executive function, and processing speed. Psychomotor slowing, also known as psychomotor retardation, refers to reduced processing speed and motor activity, such as in speech and fine- and gross-motor skills. Psychomotor slowing is a common feature of severe depression. First-line treatment of major depression includes pharmacotherapy, with or without psychotherapy. Each patient should be clinically treated and then monitored for effectiveness of therapy, continued need for pharmacotherapy, and response of cognitive symptoms.

Carbidopa-levodopa is an effective medication for symptomatic treatment of Parkinson disease (PD). This patient exhibits psychomotor slowing but lacks the decremental response (decreased speed and amplitude) on repetitive movements typical of PD and also other defining features of PD. This medication is not effective in treating major depression.

Donepezil is a cholinesterase inhibitor that can be effective in improving cognitive symptoms and function in patients with Alzheimer disease. This patient's history and results of cognitive testing are not consistent with a diagnosis of dementia. Although depression can represent a prodrome to PD, Alzheimer disease, and other neurodegenerative conditions and often accompanies these conditions, cholinesterase inhibitors are not effective in treating major depression.

Depression is often unrecognized and undertreated in the elderly and is not a consequence of normal aging. Late-life depression has been associated with an increased risk of dementia and should be treated aggressively. Therefore, clinical observation is insufficient as management.

Question 24

A 27-year-old woman is evaluated for a severe migraine with typical aura and right-sided sensory symptoms that occurred 1 day ago. Migraine was diagnosed at age 13 years, is often preceded by 45 minutes of visual loss (which she describes as “losing half my sight”), is only associated with onset of menses, involves hemicranial throbbing pain associated with nausea and vomiting, and lasts 90 minutes if treated and 24 hours if untreated. Yesterday's migraine was again preceded by the typical visual loss and 40 minutes later by numbness and paresthesia in the right upper extremity, starting in her hand and migrating toward her forearm; these sensations eventually involved her right tongue and throat, lasted an additional 50 minutes, and then resolved completely. The patient has experienced no recurrence of symptoms in the past 24 hours. Medications are rizatriptan and a combined estrogen-progesterone oral contraceptive initiated 3 months ago at a family planning clinic.

On physical examination, blood pressure is 122/72 mm Hg and pulse rate is 66/min. All other physical examination findings, including those from a neurologic examination, are unremarkable.

Findings on a brain MRI and magnetic resonance angiogram are normal.

Which of the following is the most appropriate next step in management?

A
Administer daily aspirin

B
Administer daily topiramate

C
Discontinue combined oral contraceptive

D
Discontinue rizatriptan

Answer & Critique

Correct Answer: C

Educational Objective: Treat migraine with typical aura.

Key Point

Because women with migraine with aura have an increased risk of stroke, estrogen-containing oral contraceptives, which further increase stroke risk, should be avoided.

The patient should discontinue taking the combined oral contraceptive. She has a history of migraine with typical aura. Aura is considered typical if it involves any combination of visual, hemisensory, or language dysfunction, with sensory auras most typically affecting the face and upper extremities. Each neurologic feature of a typical aura typically lasts between 5 and 60 minutes before completely resolving and can occur before, during, or independent of a headache. Migraine with typical or other aura is a strong contributor to stroke risk in women. Data suggest that migraine with aura represents the second greatest risk factor for stroke in women (after hypertension), surpassing even diabetes mellitus. Estrogen-containing contraceptives, which further increase stroke risk, should be avoided by women with this diagnosis. Progesterone-only oral contraceptives, injections, implants, and intrauterine devices do not appear to increase the risk of stroke in these patients and are preferred means of contraception in this population.

Findings from physical examination and neuroimaging studies showed no evidence of a stroke in this patient. Therefore, aspirin therapy is unnecessary.

Topiramate is approved for use as migraine prophylaxis. Because this patient typically has a migraine only at onset of menses that is successfully treated with rizatriptan, she has no need for migraine preventive therapies.

Although basilar migraine and hemiplegic migraine are contraindications for triptan therapy, this patient has no symptoms indicating the presence of either subtype. Discontinuation of rizatriptan is thus unnecessary.

Question 25

A 54-year-old man is seen for follow-up evaluation of a tremor in his upper extremities that has been present since age 20 years. The tremor was mild for many years and did not interfere with his work but has become more prominent in recent years. He has difficulty writing and using utensils during meals. He has no associated slowness, stiffness, or change in gait. The patient started a trial of propranolol, which provided better control of the tremor, but after a few months, the tremor again worsened. He has subsequently been taking clonazepam without significant relief of symptoms. Alcohol, which the patient uses infrequently, temporarily diminishes the tremor. He also has kidney stones and glaucoma. His father and two sisters have a similar tremor.

On physical examination, vital signs are normal. A persistent large-amplitude tremor of the upper extremities is noted when the patient holds his arms in an outstretched position and during finger-to-nose testing. The tremor is bilateral and absent at rest. Tandem gait cannot be performed, but gait is otherwise normal.

Which of the following is the most appropriate next step in treating this patient's tremor?

A
Botulinum toxin

B
Deep brain stimulation

C
Levodopa

D
Primidone

E
Topiramate

Answer & Critique

Correct Answer: D

Educational Objective: Treat essential tremor.

Key Point

In patients with essential tremor, propranolol and primidone are FDA approved first-line therapies.

This patient should begin a trial of primidone for his worsening essential tremor. His long history of a bilateral action tremor, family history of tremor, and ethanol responsiveness are consistent with familial essential tremor. Although the severity of this type of tremor remains stable over a lifetime in most patients, a few experience tremor progression that can become disabling. Primidone and propranolol are FDA-approved first-line treatments of essential tremor. Because propranolol has already been administered without lasting relief, a trial of primidone is warranted.

Botulinum toxin injections can be effective in patients with essential tremor of the voice and head, but its benefit is more limited in the limbs because of the adverse effect of weakness. In this patient, primidone should be initiated first.

In patients with severe medication-refractory essential tremor, deep brain stimulation (DBS) of the thalamus is most likely to maximize tremor control. However, this option should be reserved for those who have not responded to medical therapy or have a marked disabling tremor. In this subset of patients, DBS has the potential to provide significant tremor control beyond that offered by the best medical therapy. DBS is premature for this patient who has not yet had a trial of primidone.

This patient does not have features of Parkinson disease, such as a tremor at rest. Therefore, levodopa therapy is not indicated.

Topiramate is a second-line treatment of essential tremor but is contraindicated in a patient with a history of kidney stones and glaucoma.

Question 26

A 68-year-old man is evaluated in the hospital for midback pain and right leg weakness. A radiograph of the thoracic spine obtained in the emergency department showed a lytic lesion at T7, and an MRI showed extension of an associated mass lesion into the epidural space, which is causing compression of the spinal cord without spinal instability. His only medication is a daily multivitamin.

High-dose glucocorticoids are administered, and results of a stereotactic biopsy of the mass show a plasmacytoma.

On physical examination, temperature is 37.2 °C (99.0 °F). Other vital signs and findings of a general physical examination are normal. Sensory level is to T8.

Which of the following is the most appropriate next step in treatment?

A
Chemotherapy

B
Continued high-dose glucocorticoids only

C
Radiation therapy

D
Surgery

Answer & Critique

Correct Answer: C

Educational Objective: Treat compressive spinal cord lesions due to plasmacytoma.

Key Point

Spinal cord compression by skeletal lesions resulting from plasmacytoma should be treated initially with radiation therapy in patients with no spinal instability and only minor neurologic deficits.

This patient should undergo external beam radiation therapy for his epidural plasmacytoma in addition to continued high-dose glucocorticoid treatment. Skeletal lesions that occur as a result of plasmacytoma or myeloma are exquisitely radiosensitive; therefore, radiation therapy is the most appropriate specific and definitive treatment for this tumor type. Patients with compressive myelopathy due to very radiosensitive tumors who have a stable spine and minimal neurologic deficits may respond to this therapy, with recovery or improvement of their neurologic deficits.

Although radiation therapy is the preferred acute treatment for compressive myelopathy in patients with plasmacytomas because of their high level of radiosensitivity and rapid response to treatment, chemotherapy may be a reasonable second-line therapy for selected patients with compressive myelopathy due to myeloma.

High-dose intravenous glucocorticoids administered within the first 8 hours of traumatic spinal cord injury can be useful in the short term to reduce the effect of edema within the spinal cord caused by a compressive injury. However, these drugs will not treat the underlying neoplastic disease and thus are inappropriate as monotherapy in this patient.

Immediate surgical decompression is indicated with evidence of spinal instability or with severe neurologic deficits that require removal of the bulk of the tumor to prevent continued injury to the spinal cord. This intervention is usually followed by definitive radiation therapy for treatment of the local tumor.

Question 27

A 34-year-old man is evaluated in the emergency department for worsening headache, nausea, and two episodes of vomiting 2 hours after hitting his head in a fall from the top of a 6-foot ladder.

On physical examination, temperature is normal, blood pressure is 128/84 mm Hg, pulse rate is 86/min, and respiration rate is 14/min. The patient's Glasgow Coma Scale score is 15/15.

Which of the following is the most appropriate immediate step in management?

8%

A
Head CT with contrast

85%

B
Head CT without contrast

7%

C
Hospital observation

1%

D
MRI of the brain

Answer & Critique

Correct Answer: B

Educational Objective: Evaluate traumatic brain injury with CT of the head.

Key Point

Head CT without contrast is the appropriate imaging procedure for selected patients with acute traumatic brain injury.

This patient should have CT of the head without contrast. The American College of Emergency Physicians and the Centers for Disease Control and Prevention have published guidelines for management of mild traumatic brain injury (TBI). Their recommendation is to consider a noncontrast head CT in patients with TBI who have had no loss of consciousness or posttraumatic amnesia but have a focal neurologic deficit, vomiting, severe headache, physical signs of a basilar skull fracture, Glasgow Coma Scale score less than 15, coagulopathy, or a dangerous mechanism of injury, such as ejection from a motor vehicle or a falling from a height of more than 3 feet. This patient sustained a TBI with a dangerous mechanism of injury several hours ago and has developed symptoms (worsening headache and vomiting) mentioned in the guideline. Therefore, noncontrast CT of the head is indicated. A finding of parenchymal, subdural, or epidural hemorrhage requires emergent neurosurgical evaluation and consideration of possible hematoma evacuation.

In the setting of acute head trauma, head CT without contrast is preferable to head CT with contrast and brain MRI because of its lower cost and wider availability. Contrast administration aids in the assessment of certain malignant and vascular lesions of the brain but adds nothing to the evaluation of acute head trauma. Head CT without contrast is also very sensitive for detecting skull fracture or acute hemorrhage, and a CT scan generally requires shorter examination times than a brain MRI requires, both important factors in the evaluation of a patient with acute head injury and symptoms of potential deterioration.

Hospital observation without first ruling out intracranial hemorrhage is inappropriate management of TBI. Untreated intracranial hemorrhage can lead to an accumulation of blood and edema within

the skull, which can cause compression or destruction of brain tissue, increased intracranial pressure, and even herniation and death.

Question 28

An 82-year-old woman is seen for follow-up evaluation of Alzheimer disease. Since her last visit 12 weeks ago, she has been taking rivastigmine, with a progressively titrated dosage. The patient's only new symptoms are increasing insomnia, loss of appetite, and occasional diarrhea; she has had no feelings of hopelessness, helplessness, sadness, or guilt. Her only other medication is hydrochlorothiazide for hypertension.

On physical examination, vital signs are normal. The patient has lost 6.8 kg (15.0 lb) since her last visit. She scores 20/30 on a Mini–Mental State Examination, losing points in the recall, orientation to time, complex commands, and attention and calculation sections; her score 12 weeks ago was 21/30. All other findings from the general physical and neurologic examinations are normal.

Results of laboratory studies, including a complete blood count, comprehensive metabolic profile, and thyroid function tests, are normal.

Which of the following is the most appropriate next step in management?

A
Add donepezil

B
Add memantine

C
Add mirtazapine at bedtime

Discontinue rivastigmine Disc

Answer & Critique

Correct Answer: D

Educational Objective: Recognize adverse effects of cholinesterase inhibitors in a patient with Alzheimer disease.

Key Point

Gastrointestinal adverse effects can occur with cholinesterase inhibitor therapy.

This patient should stop taking rivastigmine. Given the results of her cognitive testing, she meets criteria for Alzheimer disease of mild severity. She began taking oral rivastigmine, a cholinesterase inhibitor, 12 weeks ago. All of the available cholinesterase inhibitors are approved for mild to moderate Alzheimer disease, except donepezil, which is also approved for the severe stage. Studies of cholinesterase inhibitors and memantine show consistent improvement on measures of cognition and global assessment of dementia, but the effect size is modest and evidence that they improve long-term outcome is lacking. In practice, individual response is variable. There is insufficient evidence to support one cholinesterase inhibitor over another, and choice of treatment in a patient should be based on cost, tolerability, and ease of using the specific formulation. There is also insufficient evidence of the optimal duration of treatment or when therapy should be discontinued. Medication decisions should be made on an individual basis. Cholinesterase inhibitors should be used with caution in patients with cardiac conduction abnormalities, active peptic ulcer disease (because of the risk of bleeding), and seizures. Gastrointestinal adverse effects are common to all cholinesterase inhibitors and include loss of appetite, weight loss, nausea, vomiting, and diarrhea. Insomnia also can occur. This patient has had a significant amount of weight loss, loss of appetite, and insomnia since starting rivastigmine. The most appropriate next step in management would be to discontinue the medication. A trial of a different type of cholinesterase inhibitor could be considered, but only after symptoms subside.

Donepezil, another cholinesterase inhibitor, might be considered as an alternative therapy for this patient. However, no indication supports prescribing multiple cholinesterase inhibitors concomitantly, and rivastigmine should be discontinued as the first step.

Memantine is a noncompetitive *N*-Methyl-D-aspartate receptor antagonist approved by the FDA for the treatment of moderate to severe Alzheimer disease. Although this drug could be added in the future, this patient's present symptoms should be addressed first.

Mirtazapine is a nonselective ?$_2$-adrenoceptor antagonist effective in the treatment of depression. Stimulation of appetite, weight gain, and somnolence are frequently associated effects, and thus this medication may be the preferred treatment for depressed patients with Alzheimer disease who have insomnia or loss of appetite. This patient has apathy and loss of interest, which are common symptoms in Alzheimer disease, but lacks additional symptoms to suggest depression.

Question 29

A 42-year-old woman is evaluated for progressive difficulty with eyelid closure. She initially noticed frequent blinking 3 years ago; within the past year, she also began having unintended, prolonged, and forceful closure of both eyes that now prevents her driving. Bright light, prolonged conversation, and psychological stress aggravate her symptoms. The severity of symptoms fluctuates from day to day, but she does not have any symptom-free days. She reports occasional blurry vision but has had no visual field loss or diplopia, has no sensory numbness, and has had no other abnormal movements involving the face, head, limbs, or trunk.

On physical examination, vital signs are normal. Examination of the eyes shows repetitive and bilateral clonic eyelid closures that occasionally involve forceful closure of the eyes that the patient cannot resist or suppress. The intensity of these movements varies during the examination. No facial grimacing, asymmetry, or other abnormal movements are noted. Other findings of the general medical and neurologic examinations are normal.

An MRI of the brain is unremarkable.

Which of the following is the most appropriate treatment?

A
Botulinum toxin

B
Clonidine

C
Deep brain stimulation

D
Risperidone

Answer & Critique

Correct Answer: A

Educational Objective: Treat blepharospasm with botulinum toxin in a patient with focal dystonia.

Key Point

Botulinum toxin injection is the most effective treatment of focal forms of dystonia, including blepharospasm.

Botulinum toxin injection is the most effective treatment of focal forms of dystonia, including the blepharospasm experienced by this patient. Blepharospasm is characterized by involuntary and sustained contraction of the orbicularis oculi muscle. Similar to other forms of dystonia, this condition is a result of a dysregulation within a network that involves the basal ganglia, sensorimotor centers, and the cerebellum. Blepharospasm should be distinguished from hemifacial spasm, a form of focal myoclonus resulting from irritation of the facial nerve (cranial nerve VII). Hemifacial spasm is unilateral, involves other facial nerve–innervated muscles, is associated with blinking tics that are suppressible, and usually does not lead to sustained eyelid closure.

Clonidine is appropriate to treat tics but not blepharospasm. Tics are characterized by brief and typically suppressible movements that are distinct from the sustained and forceful contractions seen in dystonia.

Deep brain stimulation for dystonia should be considered only in the treatment of medication-refractory or severe generalized dystonia. Its utility in focal and segmental dystonias is less clear, and treatment with botulinum toxin, with or without other medications, should be attempted first.

Risperidone, an atypical antipsychotic agent, is not effective against dystonic movements and may aggravate them.

Question 30

A 44-year-old man is evaluated for a 6-month history of a persistent burning sensation in the feet. He has had no numbness or weakness. Medical history is significant for hyperlipidemia. His only medication is simvastatin.

On physical examination, blood pressure is 145/85 mm Hg sitting and 130/70 mm Hg standing, pulse rate is 75/min sitting and 65/min standing, and respiration rate is 14/min; BMI is 33. Mild red discoloration and sweating of both palms are noted. Cranial nerve examination findings are normal, motor strength is intact, deep tendon reflexes are normal, and no sensory deficit to light touch, pinprick or vibration is noted. Deep tendon reflexes and gait are normal.

Results of laboratory studies include normal fasting plasma glucose, hemoglobin A_{1c}, vitamin B_{12}, and folate levels.

An electromyogram shows no evidence of neuropathy or myopathy.

Which of the following is the most appropriate diagnostic test to perform next?

A
Glucose tolerance test

B
MRI of the lumbosacral spine

C
Serum vitamin D measurement

D
Sural nerve biopsy

Correct Answer: A

Educational Objective: Diagnose small-fiber neuropathy associated with impaired glucose tolerance.

Key Point

Impaired glucose tolerance is an underlying cause of distal peripheral neuropathies, especially those involving the small fibers that carry sharp pain, temperature, and autonomic nerve fibers

This patient should have a glucose tolerance test. He most likely has small-fiber neuropathy, a condition sometimes associated with impaired glucose tolerance. Although many classic neuropathies associated with diabetes mellitus occur later in the course of the disease, impaired glucose tolerance is being increasingly recognized as an underlying cause of distal peripheral neuropathies, especially those involving the small fibers, which are unmyelinated peripheral nerves that carry sharp pain, temperature, and autonomic nerve fibers. Pure small-fiber neuropathy can present with distal upper and lower extremity pain and paresthesia without sensory or motor deficit. Autonomic deficits also may be present. Clinical examination findings are typically normal, including normal results on sensory, motor, and reflex testing with the possible exception of a mild distal sensory deficit. Results of electromyography (EMG), which assesses the large nerve fibers, can be normal. The presence of glucose intolerance should be confirmed by a glucose tolerance test.

Given the normal results of the clinical examination and EMG, an MRI of the lumbosacral spine to assess for myelopathy and radiculopathy is not warranted.

Although vitamin D deficiency can cause myopathy and central nervous system–related symptoms, it usually does not cause small-fiber neuropathy. Although multiple other conditions may be associated with small-fiber neuropathy, impaired glucose metabolism is one of the most common causes, and evaluating for this possibility should be the initial investigation. Further evaluation of small-fiber neuropathy should consider the possibility of vitamin B_{12} deficiency, HIV infection, amyloidosis, Sjögren syndrome, paraproteinemia, celiac disease, and sarcoidosis.

Sural nerve biopsy has low sensitivity in detecting small-fiber disorders. The diagnosis is instead made on the basis of autonomic testing, including quantitative sudomotor axon reflex testing and skin biopsy, to assess intraepidermal nerve fiber density.

Question 31

A 40-year-old man is reevaluated for a 1-year history of recurrent tonic-clonic seizures that have not responded to treatment with valproic acid and topiramate. When describing the seizures, his wife says that he usually drops to the ground and begins “shaking all over”; the shaking typically lasts 10 to 15 minutes, with the patient's eyes remaining closed during the event. He subsequently is confused for 30 to 60 minutes. The seizures initially occurred 1 or 2 times per month but recently have been occurring every other day. On several occasions, he has become incontinent. He is a military veteran who sustained a closed head injury in combat 5 years ago and has posttraumatic stress disorder. Medications are twice daily valproic acid and topiramate.

On physical examination, vital signs are normal. General medical examination findings are normal. On neurologic examination, flattening of the nasolabial fold on the right is noted, and right pronator drift is present. Deep tendon reflexes are 3+ in the right upper and lower extremities. A plantar extensor response is noted in the right toe.

Results of laboratory studies are normal, with a serum valproic acid level within the therapeutic range.

An MRI of the brain reveals left frontal lobe encephalomalacia. An electroencephalogram (EEG) shows intermittent left frontal slowing.

Which of the following is the most appropriate management?

A
Ambulatory EEG monitoring

B
Carbamazepine

C
Levetiracetam

D
Video EEG monitoring

Answer & Critique

Correct Answer: D

Educational Objective: Diagnose nonepileptic seizures.

Key Point

Video electroencephalography, performed in an epilepsy-monitoring unit, enables correlation of the patient's behavior with seizure activity on an electroencephalogram, which can lead to better characterization of seizure activity or allow assessment of potential non–seizure-related behaviors suggestive of nonepileptic seizures.

This patient should have continuous video electroencephalographic (EEG) monitoring for further evaluation of the seizures, which have become increasingly frequent and have not responded to two antiepileptic drugs (AEDs). Video EEG monitoring, performed in an epilepsy-monitoring unit, enables correlation of patient behavior with seizure activity on an electroencephalogram. This can lead to better characterization of seizure activity, such as the identification of specific localizing features, and allow assessment of potential non–seizure-related behaviors suggestive of nonepileptic seizures. This patient has several risk factors for psychogenic nonepileptic events. The long duration of the episodes is more typical of nonepileptic than epileptic seizures, as is the fact that his eyes remain closed during the event. The presence of incontinence does not exclude a nonepileptic episode. Although his previous closed head injury puts him at risk for epileptic seizures, it does not exclude the possibility of nonepileptic events. In fact, combat veterans, particularly those with posttraumatic stress disorder (PTSD), are at high risk for nonepileptic seizures. This diagnosis can be overlooked if a history of head trauma is present. Because epileptic and nonepileptic seizures can coexist in the same patient, a thorough description and characterization of the seizures are essential and best achieved by admission to an epilepsy monitoring unit.

Ambulatory EEG monitoring allows more prolonged evaluation of brain activity outside a clinical setting and may be helpful in identifying seizures or interictal epileptiform activity that may not have been seen on a routine interictal EEG study. However, inpatient video EEG monitoring allows analysis of both clinical and EEG characteristics of seizures to assist in diagnosis and management. The latter study is required for a diagnosis of nonepileptic seizures and presurgical

evaluations in patients who have not responded to two or more AEDs. The inpatient setting also allows for withdrawal of AEDs in a monitored environment.

A definitive diagnosis is necessary before adding more AEDs, such as carbamazepine or levetiracetam. Furthermore, levetiracetam should be avoided in this patient with PTSD because it can exacerbate anxiety and irritability.

Question 32

A 50-year-old man is evaluated for a 1-year history of increasing urinary frequency and urgency and occasional urge incontinence. He has no symptoms of urinary hesitancy or incomplete emptying. The patient has primary progressive multiple sclerosis. Medications are dalfampridine and vitamin D.

On physical evaluation, temperature is 36.8 °C (98.2 °F), blood pressure is 120/55 mm Hg, and pulse rate is 68/min. Findings of abdominal and digital rectal examinations are normal. Finger-to-nose testing reveals dysmetria bilaterally. Leg tone is increased bilaterally. Muscle strength is 4/5 in both legs. Gait testing reveals spasticity and ataxia.

A urinalysis is negative for infection.

Which of the following is the most ap propriate treatment?

A
Finasteride

B
Intermittent urinary catheterization

C
Oxybutynin

D
Prophylactic antibiotic

Answer & Critique

Correct Answer: C

Educational Objective: Treat urinary dysfunction in multiple sclerosis.

Key Point

In patients with multiple sclerosis, anticholinergic agents reduce the intensity and frequency of bladder spasms and thus may reduce symptoms of urgency, frequency, and incontinence.

This patient should be treated with an anticholinergic medication, such as oxybutynin, for bladder spasticity due to myelopathy from multiple sclerosis (MS). Several different patterns of bladder dysfunction are associated with MS, with urge incontinence due to uninhibited detrusor function caused by denervation at the level of the spinal cord being the most common. This form of bladder dysfunction responds well to anticholinergic medications, which reduce the intensity and frequency of bladder spasms and reduce urgency, frequency, and incontinence. Other forms of dysfunction include bladder inactivity (leading to overflow incontinence), the loss of the sensation of bladder fullness, and other sensory deficits that also may impair bladder emptying. These conditions are more difficult to treat because anticholinergic agents can worsen urinary retention and lead to predisposition to urinary tract infection. Patients with mixed bladder symptoms may require further diagnostic testing to better delineate the cause of incontinence.

Finasteride is a 5?-reductase inhibitor used to treat benign prostatic hyperplasia (BPH) and would have no effect on bladder spasticity. This patient is unlikely to have BPH given the normal findings on digital rectal examination and the absence of urinary hesitancy.

Intermittent urinary catheterization also has no role in isolated bladder spasticity. This patient had no symptoms or signs of urinary retention, which would be relieved by catheterization. It may, however, have a role in selected patients with complex bladder dysfunction due to MS who are not appropriate candidates for or do not respond to medical therapy.

Although patients with bladder dysfunction are at increased risk for urinary tract infection, assessing the type of bladder dysfunction present and providing appropriate treatment are indicated. Prophylactic antibiotics would not be indicated as management of this patient's urinary

incontinence in the absence of evidence of infection or recurrent infections due to bladder dysfunction refractory to therapy.

Question 33

An 80-year-old man is evaluated for a 5-year history of progressive cognitive decline. According to his daughter, his cognitive difficulties began after a series of “ministrokes” characterized by the acute onset of slurred speech, difficulty ambulating, and weakness; these symptoms typically improved after onset but never resolved entirely. He recently has had difficulty managing his financial affairs, completing tasks, and understanding abstract concepts; other recent symptoms include a slowed reaction time, slowness in speaking and completing tasks, shuffling of gait, urinary incontinence, and sudden involuntary laughing and crying. The patient has hypertension, coronary artery disease, depression, and hyperlipidemia. Medications are lisinopril, aspirin, bupropion, and atorvastatin.

On physical examination, vital signs are normal. Other findings from the general physical examination are unremarkable. Neurologic examination reveals mild right-sided weakness, right-sided hyperreflexia, and difficulty initiating forward movement of the feet (“magnetic gait”).

An MRI of the brain shows extensive periventricular white matter lesions and small-vessel disease involving the basal ganglia. The ventricles are normal in size.

Which of the fo llowing is the most likely diagnosis?

A
Alzheimer disease

B
Normal pressure hydrocephalus

C
Parkinson disease dementia

D
Vascular neurocognitive disorder

Answer & Critique

Correct Answer: D

Educational Objective: Diagnose cognitive impairment due to cerebrovascular disease.

Key Point

Widely accepted clinical criteria for diagnosing vascular neurocognitive disorder require evidence of a cognitive disorder plus a previous clinical stroke or neuroimaging evidence that confirms the existence of cerebrovascular disease.

This patient most likely has cognitive impairment due to cerebrovascular disease, otherwise known as vascular neurocognitive disorder (VND). VND comprises a group of pathophysiologically distinct processes and thus has heterogeneous clinical presentations. Because it encompasses a continuum of cognitive disorders, from mild cognitive impairment to dementia, that result from cerebrovascular disease, validated diagnostic criteria do not exist. Widely accepted clinical criteria require evidence of a cognitive disorder plus a previous clinical stroke or neuroimaging evidence that confirms the existence of cerebrovascular disease. A relationship between the cognitive decline and cerebrovascular disease should exist, as it does with this patient. The description of the “ministrokes” experienced by this patient is consistent with a history of previous lacunar strokes. Supportive features include gait disturbance, pseudobulbar affect (a neurologic disorder characterized by involuntary outbursts of laughing and/or crying that are out of proportion to the emotions being experienced), incontinence, depression, and focal neurologic signs. Cognitive impairment generally is characterized by executive dysfunction, slowed mental processing, and impaired attention, as is exhibited by this patient.

Coexisting Alzheimer disease is found at autopsy in a large number of patients with VND. However, the lack of prominent memory impairment, presence of focal neurologic symptoms and signs, and stepwise decline seen in this patient are more consistent with a clinical diagnosis of VND than Alzheimer disease.

Although this patient has some overlapping features typically associated with normal pressure hydrocephalus, such as urinary incontinence, magnetic gait, and cognitive decline, he lacks the neuroimaging findings of enlarged ventricles or hydrocephalus typically seen in this disorder.

This patient has some findings consistent with Parkinson disease, such as shuffling gait and executive dysfunction, but lacks other typical examination findings, such as asymmetric parkinsonism, resting tremor, stooped posture, and decline in fine motor movements. Underlying Parkinson disease is thus unlikely to be the cause of his symptoms.

Question 34

An 80-year-old man is evaluated for a 2-year history of sudden-onset episodes of flashing lights in the right visual field that typically last 10 to 20 seconds. He does not believe that he loses awareness during these events, but his daughter, who accompanied him, reports that he stared and smacked his lips during the two recent episodes she witnessed. Symptoms started 6 months after he had a cryptogenic stroke of the left occipital lobe. The patient also has hypertension. Medications are aspirin, atorvastatin, and lisinopril.

On physical examination, temperature is 36.7 °C (98.0 °F), blood pressure is 140/90 mm Hg, and pulse rate is 67/min and irregular. Visual field testing reveals right homonymous hemianopia. All other findings from the general physical and neurologic examinations are within normal limits.

An MRI reveals a chronic infarct in the territory of the left posterior cerebral artery.

Which of the following is the most appropriate treatment?

A
Carbamazepine

B
Lamotrigine

C
Oxcarbazepine

D
Phenytoin

Answer & Critique

Correct Answer: B

Educational Objective: Treat an older patient with seizures.

Key Point

In older patients with seizures who are treated with an antiepileptic drug, lamotrigine, levetiracetam, and gabapentin are generally better tolerated and thus good first-line options.

This patient should be treated with the antiepileptic drug (AED) lamotrigine. He has had several episodes consistent with complex partial seizures and is at high risk for recurrent seizures and associated morbidity, given his history of a previous stroke and age greater than 65 years. Older patients generally have difficulty tolerating the many adverse effects of AEDs. Lamotrigine, levetiracetam, and gabapentin are generally better tolerated in this population and thus are good first-line options. Because these medications have fewer adverse effects, older patients are more likely to continue taking them, which increases the likelihood of seizure freedom.

Carbamazepine, oxcarbazepine, and phenytoin are less well tolerated in older patients and have lower retention and seizure-freedom rates in this population. These drugs are thus inappropriate first-line treatments for this patient. Additionally, these drugs are enzyme-inducers and have drug-drug interactions with many other medications that are taken by older patients.

Question 35

A 57-year-old man is seen for follow-up evaluation after results of a carotid ultrasound obtained to investigate a left neck bruit show a mixed density plaque at the origin of the left internal carotid artery. Stenosis is estimated to be 60% to 80%. He has had no focal neurologic symptoms or visual loss. The patient has coronary artery disease (CAD) with stable angina, hypertension, dyslipidemia, type 2 diabetes mellitus, and mild kidney failure. He has a 30-pack-year smoking history but stopped smoking 7 years ago when CAD was diagnosed. Medications are aspirin, metoprolol, lisinopril, metformin, and nitroglycerin, as needed. He was taking rosuvastatin but discontinued the medication 2 years ago after developing muscle aches.

On physical examination, blood pressure is 132/78 mm Hg, pulse rate is 78/min and regular, and respiration rate is 16/min. The left neck bruit is unchanged. Cardiopulmonary examination has normal results. All other findings from the general medical and neurologic examinations are unremarkable.

Which of the following is the most appropriate next step in management?

A
Carotid endarterectomy

B
Magnetic resonance angiography of the neck

C
Resumption of statin therapy

D
Substitution of clopidogrel for aspirin

Answer & Critique

Correct Answer: C

Educational Objective: Prophylactically treat asymptomatic extracranial carotid artery stenosis.

Key Point

Using a statin to treat patients with asymptomatic internal carotid artery stenosis is associated with a stroke risk of less than 2% per year.

This patient should be restarted on statin therapy for primary prevention of stroke and myocardial infarction. The patient has type 2 diabetes mellitus and coronary artery disease, and patients with these disorders benefit from high-intensity statin therapy to reduce the risk of atherosclerotic cardiovascular disease, including myocardial infarction and stroke. High-intensity statins also are recommended for patients with stroke or transient ischemic attack of a presumed atherosclerotic subtype (although this patient is not symptomatic). With improvements in medical therapy, particularly statins, the risk of stroke has been declining in patients with asymptomatic internal carotid artery (ICA) stenosis. In a recent study, the use of a statin in patients with this diagnosis was associated with a stroke risk of less than 2% per year. Although this patient developed apparent statin myopathy from rosuvastatin, switching to another statin less associated with statin myopathy is appropriate.

Although carotid endarterectomy may benefit some patients with greater than 60% asymptomatic ICA stenosis, its effectiveness is highly dependent on the patient's underlying risks and those associated with the procedure itself. The benefit of carotid surgery is modest in patients without symptoms, and this patient's multiple medical comorbidities make him a relatively poor surgical candidate. Some studies have suggested that additional clinical factors increase the risk of stroke further in patients with asymptomatic carotid stenosis, including rapidly progressive or greater than 80% stenosis, asymptomatic infarcts on brain imaging, or abnormal results of transcranial Doppler ultrasonography. However, the role that these factors should play in clinical decisions about treatment of asymptomatic carotid stenosis has not been established. Carotid revascularization with either endarterectomy or stenting can be considered in patients at low risk for perioperative cardiovascular morbidity.

Magnetic resonance angiography (MRA) of the neck is inappropriate in this patient because an additional diagnostic test is unlikely to change the medical management of his condition. The accuracy of MRA without contrast is likely similar to that of carotid ultrasonography.

No clear evidence supports the superiority of clopidogrel over aspirin for the primary prevention of stroke in the setting of asymptomatic ICA stenosis.

Question 36

A 47-year-old woman is evaluated in the emergency department for recurrent attacks of severe holocranial pain that began 2 days ago while she was gardening. She first experienced a rapidly progressive, global, explosive headache that lasted 30 minutes and was associated with photophobia and phonophobia. She had identical symptoms 6 hours ago and additionally had 30 minutes of visual blurring and numbness of the left face and left upper extremity. The patient has attention-deficit disorder for which dextroamphetamine was initiated 2 weeks ago. She has no significant headache history.

On physical examination, blood pressure is 130/90 mm Hg and pulse rate is 86/min. Left homonymous hemianopia is noted.

An MRI of the brain shows bilateral occipital areas of acute infarction.

Cerebrospinal fluid analysis shows 10 erythrocytes, 4 leukocytes, and normal protein and glucose levels.

Four hours after entering the emergency department, the patient has a third abrupt-onset headache with worsening visual blurring. Blood pressure is now 190/115 mm Hg, but physical examination and neuroimaging findings are unchanged.

Which of the following is the most appropriate treatment?

A
Indomethacin

B
Normalization of blood pressure

C
Tissue plasminogen activator

D
Warfarin

Answer & Critique

Correct Answer: B

Educational Objective: Treat reversible cerebral vasoconstriction syndrome.

Key Point

Normalization of blood pressure is recommended in patients with reversible cerebral vasoconstriction syndrome, which commonly presents with thunderclap headaches that recur over several days or weeks.

Normalization of blood pressure is recommended for this patient with reversible cerebral vasoconstriction syndrome (RCVS). This condition most commonly presents with thunderclap headaches that recur over several days or weeks. Thunderclap attacks may occur spontaneously or be triggered by bathing, exertion, or Valsalva maneuvers. The headaches may be complicated by focal neurologic deficits with corresponding areas of stroke, parenchymal hemorrhage, or edema visible on neuroimaging studies. The cerebrospinal fluid is typically normal or near normal. Cerebral angiographic studies reveal multifocal areas of vasospasm without evidence of aneurysm. RCVS can occur without an identifiable cause or may be associated with preeclampsia or eclampsia, exposure to certain medications (sympathomimetic agents, ergots, triptans) or blood products (transfused erythrocytes, immune globulin), or catecholamine-secreting tumors. Medications or illicit drugs are associated in up to 40% of affected patients, and women with the syndrome outnumber men at a ratio of 6:1. Migraine may be a predisposing factor. Transient neurologic deficits occur in 30% of patients with RCVS, and 10% may experience persistent deficits from parenchymal damage caused by ischemic or hemorrhagic infarctions.

No clinical trial data are available on which to base therapeutic recommendations. Conservative management, supported by expert consensus, includes headache control with analgesics, careful monitoring of blood pressure to maintain normotensive goals, and serial neurologic examinations.

Primary stabbing headache is a form of benign abrupt-onset headache that may respond to indomethacin. This type of headache typically lasts seconds, not 30 minutes as with this patient. Primary stabbing headache also occurs without visual blurring, focal numbness, or other neurologic symptoms. Although indomethacin is appropriate for treating several additional primary

headache syndromes, such as chronic paroxysmal hemicrania, evidence does not support its effectiveness in RCVS.

Because reversible vasoconstriction and not thrombosis is the responsible mechanism for RCVS, tissue plasminogen activator is not indicated in this patient. The use of calcium channel

antagonists, such as nimodipine or verapamil, is more appropriate.

No evidence suggests that anticoagulants, such as warfarin, or antiplatelet agents, such as aspirin, affect stroke risk or outcomes in RCVS. The mechanism of cerebral infarction, when present, is likely related to cerebral artery vasospasm and not thrombosis. Given this pathophysiology and the relatively high rate of hemorrhagic infarction in RCVS, antiplatelet or antithrombotic therapy has no role in disease management.

Question 37

A 45-year-old man is evaluated in the emergency department for a 3-week history of headache and impaired vision on the right side. He has not previously had frequent headaches, but the current pain has been constant and worsening since onset. The patient thinks that something is wrong with his eyesight because he has been running into or tripping over objects on the right side. He has no significant medical history and takes no medication.

On physical examination, vital signs are normal. No papilledema is noted on funduscopic examination. A slit lamp examination shows no cells in the vitreous humor. Other findings from the general medical examination are unremarkable. Neurologic examination reveals the presence of right homonymous hemianopia.

An MRI of the brain shows a lesion in the left occipital lobe that is highly suspicious for central nervous system lymphoma.

Results of laboratory studies include a normal leukocyte count and differential and no evidence of HIV antibodies.

Cytologic analysis of cerebrospinal fluid shows no malignant cells.

Which of the following is the most appropriate next step in management?

A
Bone marrow biopsy

B
Surgical biopsy of the brain lesion

C
Surgical resection of the brain lesion

D
Treatment with dexamethasone

E
Treatment with photon-beam radiation

Answer & Critique

Correct Answer: B

Educational Objective: Diagnose a primary central nervous system lymphoma.

Key Point

Pathologic analysis, usually of a brain biopsy specimen, to confirm primary central nervous system lymphoma is required before beginning treatment with methotrexate-based chemotherapy and possible whole-brain radiation.

This patient should undergo surgical biopsy of the brain lesion without resection. The MRI is suggestive of primary central nervous system lymphoma (PCNSL), a non-Hodgkin lymphoma that can affect any part of the central nervous system but commonly presents as a focal supratentorial lesion; visual symptoms are common because the tumor often involves the optic radiations. Cerebrospinal fluid (CSF) analysis can be diagnostic in up to 10% of patients, and ocular involvement may be found in 10% to 20%. However, in most patients, including this one with negative results on CSF analysis and slit lamp examination, pathologic analysis of a brain biopsy specimen is required to confirm the diagnosis. Treatment most commonly involves methotrexate-based chemotherapy and possible whole-brain radiation.

Bone marrow biopsy is not indicated in this patient. PCNSL is a whole-organ disease but is not typically systemic. Therefore, a bone marrow biopsy for diagnostic purposes would have low yield.

Because PCNSL tends to localize to a single organ system and may have multiple associated manifestations, such as diffuse brain and ocular involvement, resection of the presenting lesion is not helpful and can actually worsen patient outcomes.

Dexamethasone and similar glucocorticoids should be avoided if possible before brain biopsy in patients with suspected PCNSL because these agents can significantly decrease the yield of the biopsy. Furthermore, this patient does not have signs or symptoms of increased intracranial pressure that would necessitate urgent glucocorticoids.

Radiation is not indicated for PCNSL until after a tissue diagnosis is made and treatment with methotrexate-based chemotherapy has begun. Additionally, when patients with PCNSL receive radiation, it must be whole-brain radiation, not focal photon-beam radiation, which is more appropriate for gliomas and other primary brain tumors.

Question 38

A 57-year-old woman is evaluated in the emergency department 24 hours after new onset of left hemiparesis and left hemineglect. The patient has hypertension and functional class II New York Heart Association nonischemic heart failure. Medications are enalapril, furosemide, and metoprolol.

On physical examination, temperature is normal, blood pressure is 166/78 mm Hg, pulse rate is 68/min and irregular, and respiration rate is 12/min. A cough is noted. Cardiac examination confirms an irregularly irregular heart rhythm. Neurologic examination shows left visual and tactile extinction, left facial weakness, dysarthria, left arm and leg weakness (muscle strength, 4/5), and normal orientation and language function. She is unable to safely swallow water but can swallow thickened liquids.

Results of laboratory studies are notable for an INR of 1.1 and a serum LDL cholesterol level of 54 mg/dL (1.40 mmol/L).

A CT scan of the head shows an acute infarction in the right parietal and frontal lobes involving half of the hemisphere. An electrocardiogram (ECG) shows atrial fibrillation; an ECG obtained 1 year ago was normal. An echocardiogram shows a left ventricular ejection fraction of 50% without valvular disease or wall motion abnormalities. A chest radiograph and a carotid ultrasound show normal findings.

Which of the following is the most appropriate next step in treatment?

A
Aspirin

B
Dabigatran

C
Intravenous heparin

D
Warfarin

Answer & Critique

Correct Answer: A

Educational Objective: Treat ischemic stroke in a patient with atrial fibrillation.

Key Point

In patients with acute ischemic stroke who are ineligible for recombinant tissue plasminogen activator therapy, aspirin should be administered within 48 hours of the stroke to reduce the risk of recurrent ischemic stroke.

Aspirin should be added to this patient's medication regimen. She has had an acute ischemic stroke and has atrial fibrillation. No other obvious causes of stroke are present, and she is beyond the treatment window for recombinant tissue plasminogen activator therapy. According to two large clinical trials, aspirin administered within 48 hours of ischemic stroke onset modestly reduces the risk of recurrent ischemic stroke within the first 2 weeks without significantly increasing the risk of intracerebral hemorrhage. Administration of aspirin no later than the end of the second day after a stroke is an accepted quality-of-care core metric in primary and comprehensive stroke centers.

Anticoagulation with warfarin or a newer anticoagulant, such as dabigatran, is required to manage this patient's long-term risk of cardioembolic stroke. Some experts will initiate warfarin within 24 hours of stroke onset in medically stable patients with a small infarction, but withholding anticoagulation for 4 days to 2 weeks is typically recommended for patients with moderate to large infarctions. Until that time, patients are managed with aspirin.

In the acute ischemic stroke setting, intravenous heparin was ineffective compared with aspirin in patients with cardioembolic stroke in a randomized clinical trial. Furthermore, this patient's infarct is large enough to be associated with a risk of hemorrhaging into the bed of the infarct within the first 2 weeks of stroke.

Question 39

A 65-year-old woman is evaluated in the emergency department for a 2-day history of nausea and vomiting and a 3-week history of increasingly persistent and severe morning headaches. Breast cancer was diagnosed 8 months ago and treated with lumpectomy, radiation therapy, and chemotherapy, which she recently completed. Her most recently measured functional status was good (Karnofsky Performance Score > 70).

On physical examination, temperature is 36.7 °C (98.1 °F), blood pressure is 110/70 mm Hg, pulse rate is 95/min, and respiration rate is 18/min. The patient is awake, appropriately interactive, and fully oriented. Difficulty with tasks requiring attention, such as stating the months of the year backward, is noted. Mild bilateral papilledema is present. Increased tone of the left upper and lower extremities is noted. Deep tendon reflexes are 3+ on the left and 1+ on the right. The left toe exhibits a plantar extensor response.

Results of laboratory studies, including a complete blood count, are normal.

An MRI of the brain shows a 3- × 2- × 2-cm ring-enhancing lesion at the gray-white junction of the right frontal lobe with surrounding edema.

A recent PET scan of the body showed no evidence of metastatic disease.

Which of the following is the most appropriate next step in management?

A
Brain PET

B
Lumbar puncture

C
Surgical resection of the brain lesion

D
Whole-brain radiation

Answer & Critique

Correct Answer: C

Educational Objective: Treat a solitary metastatic brain tumor.

Key Point

Complete resection followed by radiation therapy is standard-of-care treatment of an accessible solitary brain metastasis in patients with good functional status and limited extracranial disease.

This patient should undergo surgical resection of the right frontal lesion. Her clinical history and imaging findings are most consistent with a solitary brain metastasis from the breast cancer. Standard-of-care treatment of a solitary brain metastasis in a patient with a good functional status and limited extracranial disease is complete resection of the lesion (when accessible) followed by radiation therapy. This treatment offers better symptom control, longer survival time, and longer periods of independent functional status compared with other therapies, including biopsy followed by radiation.

A PET scan of the brain is unlikely to be of additional diagnostic value in this patient whose MRI clearly reveals the lesion most likely responsible for her symptoms. MRI is more sensitive and specific than other imaging techniques in detecting the presence, location, and number of metastases.

Lumbar puncture is contraindicated in this patient with signs (papilledema) and symptoms (headache, nausea and vomiting) of increased intracranial pressure. Moreover, cerebrospinal fluid analysis is rarely diagnostic of metastatic disease. If an infectious process is also suspected, which often occurs in cancer patients, its presence can be determined by biopsy at the time of surgical resection.

Whole-brain radiation is an appropriate initial therapy for patients with multiple brain metastases but not for this patient whose single metastasis can be resected.

Question 40

A 62-year-old man is evaluated in the emergency department for a 10-day history of progressively worsening shortness of breath, a 3-month history of difficulty with swallowing at dinnertime that resolves by the morning, and a 5-month history of intermittent blurry vision and fatigue. He had a urinary tract infection 2 weeks ago that was treated with ciprofloxacin, after which the fatigue and other symptoms markedly worsened.

On physical examination, temperature, blood pressure, and pulse rate are normal; respiration rate is 24/min. Other notable findings are bilateral ptosis, diplopia with sustained horizontal gaze, nasal speech, a snarling smile, weakness of cervical flexion, and symmetric weakness of shoulder abduction, arm extension, and hip flexion that becomes more severe with repeated effort. Neurologic examination shows an awake and oriented patient with normal sensation and deep tendon reflexes; no atrophy or fasciculation is noted.

Serum magnesium level is 1.5 mg/dL (0.62 mmol/L). Results of other laboratory studies, including a complete blood count and a comprehensive metabolic profile, are normal.

The patient is admitted to the ICU, where serial respiratory measurements reveal declining vital capacity and negative inspiratory force.

Which of the following is the most appropriate emergent treatment?

A
High-dose intravenous glucocorticoids

B
Intravenous magnesium

C
Intravenous pyridostigmine

D
Plasmapheresis

Answer & Critique

Correct Answer: D

Educational Objective: Treat myasthenic crisis.

Key Point

Patients in myasthenic crisis should be treated emergently with either plasmapheresis or intravenous immunoglobulin.

Treatment with plasmapheresis should be started immediately in this patient with myasthenic crisis. His several-month history of fluctuating proximal weakness with ocular and bulbar involvement is consistent with myasthenia gravis. His rapid decline most likely has been precipitated by recent exposure to ciprofloxacin. Fluoroquinolones can decrease transmission at the neuromuscular junction and exacerbate myasthenia gravis. Although Guillain-Barré syndrome (GBS) also can present with rapidly progressive respiratory failure, the slow clinical course and preserved reflexes in this patient are not consistent with GBS.

Patients with suspected myasthenic crisis (rapid respiratory failure) should be admitted to the ICU and have their respiratory parameters (vital capacity and negative inspiratory force) closely monitored. If myasthenic crisis is confirmed, treatment should be started emergently with either plasmapheresis or intravenous immune globulin (IVIG).

High-dose glucocorticoids can initially aggravate symptoms of myasthenia gravis. These agents can be started after therapy with plasmapheresis or IVIG has been initiated.

Magnesium deficiency usually presents as neuromuscular hyperexcitability, not muscular weakness. Furthermore, because magnesium administration can exacerbate myasthenia gravis by neuromuscular junction blockade, it is inappropriate for this patient. Other medications that need to be used with caution in this setting include fluoroquinolones, aminoglycosides, ?-blockers, and calcium channel blockers.

Pyridostigmine can worsen respiratory secretions and should be avoided in the setting of acute respiratory failure with bulbar weakness.

Question 41

A 44-year-old man is evaluated for a 1-week history of severe, recurrent, left periorbital headaches. The patient has experienced a 10- to 12-week period of similar headaches every spring for the past 3 years. Headaches occur once or twice daily, last 2 to 3 hours if untreated, and are accompanied by nausea, photophobia, and ipsilateral tearing but no aura or vomiting. Resting during headache episodes brings no relief; he instead paces the floor. Simple analgesics and prednisone have been ineffective in treating the headache. Although subcutaneous sumatriptan generally relieves symptoms within 5 to 10 minutes, his headache frequency and dosing limitations preclude his using this drug every time he has symptoms. The patient has a 20-pack-year history of smoking. He takes no other medication.

On physical examination, blood pressure is 134/82 mm Hg and pulse rate is 78/min. All other physical examination findings, including those from a neurologic examination, are unremarkable.

Which of the following is the most appropriate next step?

A
Amitriptyline

B
Indomethacin

C
Propranolol

D
Topiramate

E
Verapamil

Answer & Critique

Correct Answer: E

Educational Objective: Prevent cluster headache.

Key Point

Oxygen therapy and subcutaneous sumatriptan are the most effective acute cluster headache treatments, and verapamil is the drug of choice for cluster headache prevention.

The patient should be treated with verapamil for episodic cluster headache. He experiences one or two daily attacks of severe, unilateral, periorbital pain lasting 2 to 3 hours if untreated that is accompanied by at least one ipsilateral cranial autonomic feature, such as ptosis, tearing, or rhinorrhea; he also exhibits motor restlessness during headache episodes. These features meet International Headache Society criteria for cluster headache. Cycles of cluster headache can last weeks to months, with attack frequency varying from 1 event every other day to 8 per day. Cluster headache typically affects young and middle-aged adults. Male sex and tobacco use are risk factors.

Oxygen therapy and subcutaneous sumatriptan are the most effective acute cluster headache treatments. Glucocorticoids can help reduce attack frequency and are effective as a bridge therapy to longer-term prophylactic agents. Verapamil is the drug of choice for cluster headache prevention. Because relatively high doses are sometimes required, regular electrocardiographic assessment for potential prolongation of the P-R interval or heart block is recommended.

Both amitriptyline and propranolol are effective agents for prevention of migraine but not cluster headache. The duration of the headaches described by this patient is too short to meet criteria for migraine.

Indomethacin is an effective treatment for chronic paroxysmal hemicrania (CPH) but not cluster headache. CPH also is characterized by repetitive episodes of unilateral pain with ipsilateral autonomic features but occurs at least 5 times daily with a typical duration between 3 and 20 minutes.

Anticonvulsants, such as topiramate, have limited effectiveness in cluster headache prevention and should be considered only after verapamil therapy proves ineffective or is poorly tolerated.

Question 42

A 50-year-old woman is evaluated for a 4-year history of progressively worsening cognitive function. She now has frequent memory deficits and a decreased ability to concentrate and multitask in her work as a lawyer; she has been reprimanded in recent months by her employer for submitting late and disorganized briefs. She has no other symptoms. The patient has a 15-year history of multiple sclerosis and a 5-year history of depression. She reports that her mood is good, and she is not experiencing her typical symptoms of depression, including anhedonia, depressed mood, and sleep disturbance. Medications are dimethyl fumarate, a vitamin D supplement, fluoxetine, and modafinil.

Physical examination reveals a pleasant, interactive woman. Vital signs are normal. Mild gait ataxia is noted. Mental status examination reveals moderate deficiencies in short-term memory, processing speed, and attention.

An MRI of the brain obtained 2 weeks ago showed multiple white matter lesions consistent with multiple sclerosis, with no significant change from an image obtained 1 year ago.

Which of the following is the most appropriate treatment of this patient's cognitive difficulties?

A Amantadine

B Counseling and cognitive therapy

C Donepezil

D High-dose intravenous methylprednisolone for 5 days

E Increased fluoxetine dosage

Answer & Critique

Correct Answer: B

Educational Objective: Treat cognitive dysfunction in multiple sclerosis.

Key Point

Formal neuropsychological testing, counseling, cognitive therapy, and accommodative strategies (such as creating checklists to overcome memory deficits) sometimes can be of benefit in patients with cognitive dysfunction related to multiple sclerosis.

This patient should be referred for counseling and cognitive therapy. Cognitive dysfunction is a common symptom in multiple sclerosis (MS), occurring in at least 50% of affected patients. The most common deficits involve short-term memory, processing speed, and executive function. This cognitive disability can have a significant effect on employment of patients with MS and can reduce their overall quality of life. Unfortunately no trials of pharmacologic therapy to reduce or prevent cognitive dysfunction in MS have as yet been successful. Formal neuropsychological testing, counseling, cognitive therapy, and accommodative strategies (such as creating checklists to overcome memory deficits) sometimes can be of benefit.

Amantadine is an appropriate treatment of the fatigue associated with MS but has not been shown to improve cognitive function in this disorder.

Donepezil has shown benefit for mild to moderate cognitive dysfunction due to Alzheimer disease. However, a randomized placebo-controlled trial of this medication in patients with MS who also had cognitive dysfunction showed no cognitive benefit.

The use of high-dose intravenous methylprednisolone is indicated only for acute exacerbations of MS, which the patient is not experiencing. The MRI also shows no evidence of breakthrough inflammatory activity.

Increasing the patient's fluoxetine dosage will not affect her cognition. Although depression is a common symptom in MS, and severe depression can be associated with a pseudodementia-like state, the patient did not report any worsening of depression and has a normal affect.

Question 43

A 41-year-old man is evaluated for daily headaches. The patient has had migraine with aura since age 15 years and had a mild traumatic brain injury while playing intramural football at age 22 years. Over the past 10 years, migraine frequency has increased from monthly to several days per week. He describes migraine episodes as global, throbbing, and severe in intensity, noting they are often accompanied by nausea, vomiting, and photophobia and sometimes preceded by 30 minutes of visual scintillations. Migraine duration is typically 2 hours with successful treatment. He takes oral sumatriptan as needed for migraine and typically uses his entire monthly allotment; propranolol was added for migraine prophylaxis 2 months ago with no appreciable effect. Ever since lumbar pain with radiculopathy was diagnosed 6 months ago and treated with hydrocodone 3 or 4 days each week, he also has developed a daily, constant, mild bilateral frontotemporal “squeezing” headache associated with maxillary pressure and neck tightness. He occasionally uses the hydrocodone to treat the headaches.

On physical examination, blood pressure is 120/72 mm Hg and pulse rate is 60/min; BMI is 28. Neurologic examination findings are normal, as are other physical examination findings.

A CT scan of the head is normal.

Which of the following is the most likely diagnosis?

A
Chronic posttraumatic headache

B
Chronic tension-type headache

C
Idiopathic intracranial hypertension

D
Medication overuse headache

Answer & Critique

Correct Answer: D

Educational Objective: Diagnose medication overuse headache.

Key Point

Medication overuse headache requires the presence of a headache-susceptible patient and excessive exposure to a causative medication, such as an opioid analgesic.

This patient has developed medication overuse headache, which requires the presence of a headache-susceptible patient and excessive exposure to a causative medication. This patient has an underlying history of migraine treated with sumatriptan, and he has been exposed to hydrocodone for back pain. The use of opioid analgesics more than 10 days per month can contribute to the development of medication overuse headache. Daily analgesic exposure is not required. Patients with this condition may develop a worsening of their underlying headache disorder or a new milder, nonspecific headache.

Posttraumatic headaches have been reported to occur in as many as 70% of persons after mild traumatic brain injury (TBI). Posttraumatic headache types are classified similarly to nontraumatic headaches, with migraine and tension-type headaches being the most prevalent. Although this patient has a history of mild TBI, the timing of the TBI and the timing of the headache have no correlation. A true posttraumatic headache must develop within 7 days of the injury.

The headaches described by this patient have phenotypic features of chronic tension-type headache. However, this diagnosis requires the exclusion of secondary headache disorders, such as medication overuse headache, and thus is premature at this time.

Given the absence of papilledema, the diagnosis of idiopathic intracranial hypertension is unlikely.

Question 44

A 35-year-old woman is evaluated in the emergency department for a 3-day history of diplopia, vertigo, and gait imbalance that has prevented her going to work. She reports no additional symptoms. The patient has multiple sclerosis, vitamin D deficiency, and depression. Medications are interferon beta-1a, vitamin D, and extended-release venlafaxine.

On physical examination, temperature is 36.5 °C (97.7 °F), blood pressure is 100/55 mm Hg, pulse rate is 72/min, and respiration rate is 14/min. Incomplete abduction of the right eye is noted when the patient looks to the right. Finger-to-nose testing with the right arm reveals dysmetria. Tandem gait testing results in a near fall.

A T2-weighted MRI of the brain shows multiple new lesions, three of which enhance after administration of intravenous contrast.

Which of the following is the most appropriate next step in treatment?

A
Glatiramer acetate

B
Intravenous methylprednisolone, 1 g/d

C
Oral prednisone, 1 mg/kg

D
Plasmapheresis

Answer & Critique

Correct Answer: B

Educational Objective: Treat a multiple sclerosis relapse.

Key Point

The standard of care for multiple sclerosis relapses is a high-dose glucocorticoid, usually intravenous methylprednisolone.

This patient should receive intravenous methylprednisolone. Her symptoms are consistent with a new multiple sclerosis (MS) relapse, most likely localizing to a new lesion in the pons and pontocerebellar pathways on the right. The standard of care for MS relapses is a high-dose glucocorticoid, usually intravenous methylprednisolone, 1 g/d for 3 to 5 days. Although this treatment has not been shown to reduce the amount of long-term disability sustained in a relapse, it substantially hastens the rate of recovery. Because of the unclear long-term benefit and the potential for adverse effects, acute high-dose glucocorticoid therapy is usually reserved for attacks resulting in sustained impairment in functional status that interferes substantially with activities of daily living.

In addition to treatment of individual relapses, most patients with relapsing-remitting MS receive chronic maintenance therapy with immunomodulatory or immunosuppressive medications, such as the interferon beta-1a that this patient takes. These disease-modifying therapies have been shown to reduce the relapse rate, slow disability progression, and reduce the accumulation of new demyelinating lesions on MRI. Glatiramer acetate is another disease-modifying drug that has been shown to reduce the relapse rate by approximately one third compared with placebo and appears equivalent to the interferon beta preparations in head-to-head studies. Combining glatiramer acetate with an interferon beta provides no added benefit compared with what either drug achieves alone. Additionally, disease-modifying medications are not effective in hastening recovery in a patient with a functionally significant acute exacerbation of MS.

Although an increasing number of studies suggest the equivalency of oral treatment with prednisone and intravenous treatment with another glucocorticoid for MS, the reported equivalent dose of prednisone is 1250 mg/d, which is a very high dose. In the original Optic Neuritis Treatment Study, which compared treatment of optic neuritis with oral prednisone (1 mg/kg),

intravenous methylprednisolone (1 g/d), or placebo, the oral prednisone group had worse outcomes after treatment than even the placebo group. Thus, oral prednisone in the range of 1 mg/kg may actually be detrimental in treating acute demyelination.

Relapses that are refractory to glucocorticoid treatment may respond to rescue therapy with plasmapheresis. Since this patient has not received a trial of intravenous methylprednisone, treatment with plasmapheresis is premature.

Question 45

An 82-year-old man is evaluated in the hospital for right-sided weakness and difficulty speaking. He was found in bed by his son, who last saw him well 18 hours ago. The patient does not seek routine medical care. He takes no medication.

On physical examination, blood pressure is 196/88 mm Hg, pulse rate is 84/min and regular, respiration rate is 12/min, and oxygen saturation is 98% on ambient air. Other general physical examination findings, including those from an evaluation of the fundi, are normal. Neurologic examination reveals right-sided facial weakness, severe dysarthria with an inability to swallow, right-sided arm paralysis, 3/5 muscle strength throughout the right leg, and no aphasia.

Results of laboratory studies show normal serum levels of creatinine and troponin T and I.

An electrocardiogram shows normal sinus rhythm with no ischemic changes, and a chest radiograph is normal. A CT scan of the head without contrast shows a left pontine infarct.

Which of the following is the most appropriate acute blood pressure treatment?

9%

A Administer oral captopril

6%

B Administer oral metoprolol

3%

C Administer sublingual nitroglycerin

82%

D No pharmacologic treatment is required

Answer & Critique

Correct Answer: D

Educational Objective: Manage hypertension in a patient with acute ischemic stroke.

Key Point

Treatment guidelines advise treatment of hypertension in patients with acute ischemic stroke only if blood pressure is greater than 220/120 mm Hg or evidence of other end-organ damage exists.

This patient should receive no pharmacologic treatment. He has an ischemic stroke in the pons, which is commonly caused by hypertensive changes in penetrator vessels originating from the basilar artery. He is not a candidate for intravenous thrombolysis because 18 hours have passed since he was known to be well. He has an elevated blood pressure but no evidence of end-organ damage. Treatment guidelines advise treatment of hypertension in the setting of acute ischemic stroke only if blood pressure is greater than 220/120 mm Hg or evidence of other end-organ damage exists. The rationale for these guidelines is to prevent neurologic worsening from expansion of the cerebral infarct; in recent clinical trials, acute lowering of blood pressure with candesartan within 36 hours of stroke was associated with neurologic worsening. When appropriate, antihypertensive medications are commonly started close to the day of discharge home or to a rehabilitation facility.

Neither oral captopril nor oral metoprolol is appropriate for this patient, who does not require immediate treatment of hypertension. Additionally, he should not be given any oral medication until a dysphagia evaluation documents the ability to swallow.

Sublingual nitroglycerin is also inappropriate because the patient does not require therapy to lower blood pressure at this time.

Question 46

A 53-year-old man is evaluated for persistent right-sided facial weakness. Three months ago, he first noticed “droopiness” of the right side of his lower face, difficulty closing the right eye and wrinkling the forehead, increased sensitivity to loud noises, and occasional slurred speech. Bell palsy was diagnosed, and he began a 10-day course of prednisone. He has noted only limited improvement, with continued facial drooping and mildly dysarthric speech; he now uses an eye patch over his right eye at night. The patient takes no medication.

On physical examination, vital signs are normal. Right-sided facial weakness involving the forehead, orbicularis oculi, and lower facial muscles is noted. Taste recognition is impaired on the anterior right side of the tongue. Facial sensation and the muscles of mastication are intact. The corneal reflex is present bilaterally, and the jaw reflex is normal. Hearing is intact bilaterally, as are extraocular reflexes, motor and sensory function, and deep tendon reflexes.

Which of the following is the mos t appropriate next step in management?

A
Acyclovir

B
Clinical observation

C
MRI of the brain

D
Physical therapy

Answer & Critique

Correct Answer: C

Educational Objective: Evaluate facial nerve palsy with incomplete recovery after 3 months.

Key Point

MRI of the brain is an appropriate next step in management for patients with incomplete recovery 3 months after onset of facial nerve palsy despite appropriate initial treatment.

An MRI of the brain should be obtained in this patient who has limited recovery despite appropriate treatment 3 months after onset of complete facial nerve (cranial nerve VII) palsy to rule out an underlying structural abnormality. He has acute weakness involving both upper and lower facial muscles, which favors a peripheral rather than central weakness. The initial presence of hyperacusis and the impaired taste noted on examination are also consistent with facial nerve involvement. In patients with typical isolated facial nerve paralysis, immediate brain imaging is unnecessary. Most of these patients have idiopathic Bell palsy, and 70% to 90% achieve complete recovery within 3 months. Severe residual weakness occurs in a minority of patients with Bell palsy, but the persistence of significant deficits at 3 months should prompt further investigation, including evaluation for alternative causes of facial nerve paralysis (such as diabetes mellitus, Lyme disease, vasculitis, HIV infection, sarcoidosis, paraproteinemia, and Sjögren syndrome) and an MRI of the brain to rule out structural causes. If results of this evaluation do not reveal a cause of the persistent symptoms, the diagnosis is incomplete recovery after Bell palsy, and clinical monitoring is then recommended.

Acute monotherapy with antiviral medications, such as acyclovir, does not improve prognosis. Early adjunctive use of antiviral therapy in addition to prednisone is favored by some experts, but the evidence supporting this treatment is inconsistent.

Evidence supporting the benefit of physical therapy for rehabilitation after facial nerve palsy is insufficient. In this patient, a structural cause of the deficits should first be excluded.

Question 47

A 32-year-old man is evaluated in the emergency department 2 hours after having a witnessed tonic-clonic seizure that lasted 2 minutes. After the seizure, he noted transient weakness of the right arm. The weakness has now resolved, and he feels completely normal. The patient reports that before losing consciousness, he felt a painful numbness in the first and second digits of the right hand, which subsequently assumed a "claw-like" posture. He never has had a similar sensation. He sustained a closed head injury resulting in a brief loss of consciousness 5 years ago in military combat. He takes no medication.

On physical examination, vital signs are normal. The patient's facial features are symmetric. Right pronator drift and difficulty with rapid alternating movements of the right hand are noted. Examination of the right upper extremity shows muscle strength of 4+/5 and 1+ deep tendon reflexes; muscle strength is 5/5 and reflexes are 2+ in all other limbs.

Laboratory studies, including a complete blood count, comprehensive metabolic profile, and urinalysis, have normal results.

An MRI shows encephalomalacia from his previous head trauma in the left parietal lobe and no other acute findings.

Which of the following is the most appropriate next step in management?

A
Ambulatory electroencephalographic monitoring

B
Carbamazepine

C
Clinical observation

D
Lumbar puncture

Answer & Critique

Correct Answer: B

Educational Objective: Evaluate a first seizure in a patient at high risk of recurrent seizure.

Key Point

In a patient with a first seizure and risk factors for future seizures, treatment with an antiepileptic drug is appropriate.

This patient should receive an antiepileptic drug (AED), such as carbamazepine. His seizure was unprovoked. The 2-year risk of recurrence after a single unprovoked seizure is approximately 40%. On the basis on this estimate, most experts do not recommend starting an AED for a first seizure unless the patient has risk factors that increase the likelihood for future events. This patient, however, has several risk factors for future seizures, including previous head trauma with loss of consciousness, a focal brain lesion on MRI, and postictal Todd paralysis of the right arm (focal weakness after a seizure). His risk of future seizures is high, and he should be treated with an AED. In this patient, the brain injury involving the contralateral parietal lobe is likely the source of the seizure, with the abnormal sensation experienced at seizure onset representing a sensory aura. He most likely had a simple partial seizure starting in the parietal lobe that spread to the motor cortex, which led to the dystonic posture of his hand and subsequent tonic-clonic seizure.

Ambulatory electroencephalography (EEG) is an outpatient test that can be useful to exclude the presence of unrecognized seizures and provide a more sensitive evaluation of interictal discharges than a 30-minute EEG. This test, however, is not performed in the emergency department and does not have to be completed before starting treatment in this patient, who had a witnessed seizure and has a high risk of recurrent seizure.

Clinical observation is appropriate management of a single unprovoked seizure only in patients with no risk factors for future seizures.

A lumbar puncture is indicated in some patients with a first seizure if they have symptoms or signs of infection or have altered mental status. In this patient with a clear reason for a partial seizure, a normal mental status, and no signs of infection, a lumbar puncture is unnecessary.

Question 48

A 38-year-old man is evaluated for headaches associated with visual changes. He describes intermittent headaches that began 18 years ago, occur three to four times per month, and typically last 12 to 24 hours. The pain is bifrontal, throbbing, occasionally severe, and worsened when he bends forward or ascends stairs. Headaches are accompanied by mild photophobia and phonophobia but no nausea or vomiting. Approximately twice yearly he experiences unilateral visual distortion during a headache attack that he characterizes as “looking through frosted glass”; the visual change typically lasts for only 30 to 40 minutes and then resolves completely. He has taken aspirin, acetaminophen, naproxen, and ibuprofen at various points to relieve his symptoms, but no medication has been effective in relieving either the headaches or visual distortion.

On physical examination, vital signs are normal. All other physical examination findings, including those from a neurologic examination, are unremarkable.

Which of the following is the most appropriate management?

A
CT of the head

B
Electroencephalography

C
Erythrocyte sedimentation rate measurement

D
MRI of the brain

E
Sumatriptan administration

Answer & Critique

Correct Answer: E

Educational Objective: Treat migraine with aura.

Key Point

Neuroimaging is inappropriate in the evaluation of uncomplicated headache.

The patient has migraine with aura and should be given sumatriptan. The pattern of his headaches has been stable for more than a decade and meets diagnostic criteria for migraine, namely, that migraine attacks should last between 4 and 72 hours if untreated, and the pain must possess two of the following four features: unilateral location, throbbing nature, moderate or severe intensity, and aggravation with physical activity. The quality and duration of the episodic visual distortion are compatible with migraine aura. Aura occurs in 25% to 35% of those with migraine and, most commonly, is visual. By definition, migraine aura should last between 5 and 60 minutes with complete resolution. Symptoms often precede headache but may accompany or even occur separately from the pain of an attack. Episodes of hemisensory symptoms or language disturbance of a similar duration are also described as “typical” aura and warrant no specific restrictions or acute migraine therapy. Because of their lower cost, NSAIDs are considered first-line options in acute migraine management. Because this patient has not responded to NSAIDs, acute treatment with a triptan is now appropriate.

CT of the head and MRI of the brain may be appropriate in the setting of potential secondary headache, but this patient has no “red flags” raising concern for this type of headache and instead exhibits classic signs and symptoms of migraine with aura. The headache pattern is stable, the visual loss is periodic and always reversible over the course of many years, and both headache and visual loss meet diagnostic criteria for migraine with aura. Neuroimaging is inappropriate in the evaluation of uncomplicated headache.

Similarly, electroencephalography has no role in the assessment of headache disorders, according to the American Academy of Neurology's five “Choosing Wisely” initiatives. Compared with standard clinical evaluation, it offers no diagnostic advantage, does not improve outcomes, and adds to medical costs.

Measurement of the erythrocyte sedimentation rate would be reasonable in the setting of suspected temporal arteritis. However, the young age of this patient and stable migraine pattern—episodic headaches with occasional transient visual impairment over 18 years—are incompatible with this diagnosis. Visual loss that occurs with temporal arteritis is typically monocular and more compatible with ischemic events, such as amaurosis fugax. Although the visual loss in typical migraine aura is benign and fully reversible, that noted with temporal arteritis is concerning and may become permanent following retinal artery occlusion.

Question 49

A 45-year-old man is evaluated for significant fatigue since having a lacunar stroke 6 months ago. He reports not resting well at night and feeling sleepy at work; he does not fall asleep inappropriately during the day. He has been able to maintain a daily 20-minute exercise program without difficulty. A recent electrocardiogram and echocardiogram were normal. Since his stroke, the patient has had no depressed mood and has continued to enjoy spending time with family and pursuing his hobbies. He has dyslipidemia, hypertension, and a remote history of depression. Medications are simvastatin, lisinopril, and aspirin.

On physical examination, blood pressure is 146/78 mm Hg, pulse rate is 68/min and regular, and respiration rate is 12/min; BMI is 32. Cardiac examination reveals no carotid bruits or other abnormalities. Neurologic examination shows mild dysarthria and grade 4/5 left-sided weakness throughout.

Which of the following is the most appropriate next step in management?

A
Cardiovascular stress testing

B
Citalopram

C
Dextroamphetamine

D
Polysomnography

Answer & Critique

Correct Answer: D

Educational Objective: Diagnose medical complications after stroke.

Key Point

Common reversible causes of fatigue after stroke include depression, sleep apnea of the central or obstructive type, and heart failure.

This patient should be referred for polysomnography. His chief symptom of fatigue is highly prevalent among patients in the poststroke period. Common reversible causes of fatigue after stroke include depression, sleep apnea of the central or obstructive type, and heart failure. This patient has had no recent depression and has normal findings on cardiac examination. He has an elevated BMI and hypertension, both of which are associated with sleep apnea. The diagnosis of sleep apnea is typically confirmed by polysomnography. Appropriate treatment of the sleep apnea can lead to lessening of fatigue symptoms and improved control of hypertension.

Cardiovascular stress testing is inappropriate in this patient who reports no exercise-induced fatigue and has normal findings on a recent electrocardiogram and echocardiogram. Myocardial ischemia is thus unlikely as an explanation of his symptoms. Patients with ischemic stroke are nonetheless at high risk for myocardial infarction, and a previous ischemic stroke is a coronary risk equivalent for the purposes of cardiovascular disease risk factor management strategies.

Depression is highly prevalent after stroke and is associated with poorer recovery and nonadherence to medical therapy. Use of antidepressant medications or cognitive behavioral psychotherapy (or both) is standard treatment of patients with stroke who experience depression. Although this patient has a remote history of depression, and fatigue can be a symptom of depression, he does not exhibit depressed mood or anhedonia, which are both elements of the two-question depression screening instrument. Treatment with citalopram or another antidepressant medication is therefore not necessary, although he should continue to be screened for this complication on routine visits.

Stimulants, including amphetamines, have shown no clinical benefits in stroke recovery and may exacerbate patients' hypertension. Dextroamphetamine is thus not appropriate in the management of this patient's poststroke fatigue.

Question 50

A 33-year-old woman is evaluated for a 3-day history of worsening right eye pain and a 1-day history of visual disturbance in the right eye. The pain is aggravated by eye movement. Three years ago, she experienced right arm clumsiness and a mildly unsteady gait but did not seek medical attention; symptoms fully resolved within 1 week. Medical history is otherwise unremarkable, and the patient takes no medication.

On physical examination, temperature is 36.2 °C (97.2 °F), blood pressure is 125/53 mm Hg, pulse rate is 80/min, and respiration rate is 16/min; BMI is 30. Pupillary reactivity is normal when each eye is tested individually; however, when a light is rapidly moved from the left eye to the right, the right pupil dilates by 2 mm. Visual acuity is 20/100 in the right eye and 20/20 in the left. Visual field testing reveals a central scotoma. Slight temporal disc pallor is noted on the right. Other findings from the general medical and neurologic examinations are normal.

Which of the following diagnostic tests is most appropriate to perform next?

A
Erythrocyte sedimentation rate determination

B
Lumbar puncture

C
MRI of the brain

D
Serum rapid plasma reagin test

Answer & Critique

Correct Answer: C

Educational Objective: Diagnose multiple sclerosis in a patient with optic neuritis.

Key Point

In patients with optic neuritis, an MRI of the brain should be obtained to evaluate for brain lesions consistent with multiple sclerosis, which is the most common cause.

This patient should have an MRI of the brain. She has symptoms and signs consistent with optic neuritis, including pain with eye movement, central scotoma, and an afferent pupillary defect. Although idiopathic optic neuritis can occur, the most common cause is multiple sclerosis (MS). An MRI of the brain should be obtained to evaluate for brain lesions consistent with MS. If they are present, a diagnosis of MS is likely on the basis of the official diagnostic criteria. These criteria require clinical and radiologic dissemination of lesions in space and time. In this patient, the occurrence of two disparate clinical events happening at separate times satisfies criteria for dissemination in time, and the presence of an optic nerve (cranial nerve II) lesion (detected on clinical examination) and additional brain lesions (if shown by MRI) would satisfy criteria for dissemination in space.

Determination of the erythrocyte sedimentation rate (ESR) has no role in the evaluation of MS. ESR elevation can occur in giant cell arteritis, a potential cause of visual loss, but this is typically a condition of older patients. In addition, this patient has not had the symptom of a headache.

Although a lumbar puncture is often performed when evaluating a patient for MS, the presence or absence of oligoclonal bands in the cerebrospinal fluid (CSF) is not part of any MS diagnostic criteria. Approximately 10% to 15% of patients with MS do not have these bands in their CSF, and their presence, by itself, is a nonspecific finding. If an MRI confirms the diagnosis of MS, CSF examination is unnecessary.

A rapid plasma reagin test is a screening test for syphilis. The classic pupillary abnormality of neurosyphilis is the Argyll-Robertson pupil, in which pupils are unreactive to light but constrict to accommodation. This patient instead manifested an afferent pupillary defect, which is a sign of

reduced optic nerve (cranial nerve II) conductance. Although optic nerve inflammation can be a complication of meningovascular neurosyphilis, this scenario is quite rare, and this patient shows no other concerning signs or symptoms for this condition.

Question 51

An 18-year-old man is evaluated for recurrent headaches 1 week after falling on his head during a soccer match at his high school. The patient reports being “dazed” for 15 minutes after the fall but never losing consciousness. Findings from a sideline examination were unremarkable, and the patient was removed from play. Given the temporary alteration in consciousness, a follow-up examination with his internist was recommended. He developed headaches the morning after the injury that for 3 days were severe, global, throbbing, and associated with nausea and dizziness; the nausea and dizziness have gradually resolved, and for the past 2 days, the headache pain has been controlled with acetaminophen. He has had no cognitive symptoms but has not yet resumed school or sports activities.

Results of physical examination, including vital signs and neurologic examination findings, are unremarkable.

Which of the following is the most appropriate management?

A
Obtain a CT of the head

B
Obtain an MRI of the brain

C
Prohibit contact sports

D
Restrict classroom participation

Answer & Critique

Correct Answer: C

Educational Objective: Prevent worsening of traumatic brain injury.

Key Point

Contact sports should be prohibited in patients who are symptomatic after sustaining a mild traumatic brain injury.

Contact sports should be prohibited for this patient with symptoms after sustaining a mild traumatic brain injury, which occurred when head trauma resulted in a transient alteration of neurologic function. The patient exhibited the typical physical symptoms of this type of injury, including headache, dizziness, and nausea. Although the symptoms have largely resolved, he still requires acetaminophen to control headache pain. Prohibiting contact sports is recommended for a patient who is still symptomatic. This restriction should remain in place even when the patient is in an asymptomatic state after taking medication. Not until the patient is asymptomatic without taking any medication should a return to contact sports be considered.

In the presence of normal findings on physical examination, a head CT scan or MRI of the brain is unlikely to provide any useful information and thus has no role. A noncontrast head CT scan is recommended in the setting of acute head injury when skull fracture or intracranial hemorrhage is suspected. Risk factors for these findings include prolonged loss of consciousness, posttraumatic amnesia, focal neurologic deficit(s), vomiting, severe headache, physical evidence of a basilar skull fracture, a Glasgow Coma Scale score less than 15, coagulopathy, or a dangerous mechanism of injury. MRI of the brain may be more sensitive in the detection of small areas of parenchymal damage or hemorrhage in the patient who is seen days or weeks after an injury, but suspicion of such damage would be low in this patient who has shown significant improvement 1 week after the trauma.

Gradual reintroduction of cognitive and normal physical activities is recommended for patients with concussion. Those with significant cognitive symptoms or neuropsychological examination deficits should have restrictions placed on cognitive activity. Immediate resumption of normal levels of

cognitive activity (such as full days of classroom work) may delay recovery in some patients. Typically, cognitive rest is recommended for 3 to 7 days, followed by gradual reintroduction of cognitive activity periods. These periods initially should be limited to the threshold of concussion symptom aggravation but, over time, should be lengthened. Given the wide variability of recovery timeframes, management must be individualized. In this patient without any cognitive or significant physical symptoms 1 week after the injury, returning to school is appropriate, and restriction of classroom participation is not required.

Question 52

A 29-year-old woman comes to the office to discuss her plans for pregnancy; she hopes to become pregnant before the end of the year. The patient has juvenile myoclonic epilepsy that was diagnosed 13 years ago. She started taking valproic acid at that time to treat the epilepsy and was seizure free until 1 year ago when she decided to stop taking the valproic acid and had a convulsive seizure. After resuming the medication, she has been otherwise asymptomatic except for occasional brief jerks of her hands that occur in the morning when she is sleep deprived but at no other time. Medications are valproic acid and folic acid.

All physical examination findings, including vital signs and results of a neurologic examination, are normal.

In addition to discontinuing valproic acid, which of the following is the most appropriate next step in treatment?

A
Begin carbamazepine

B
Begin levetiracetam

C
Begin topiramate

D
Withhold AED therapy until after pregnancy

Correct Answer: B

Educational Objective: Treat generalized epilepsy in a woman of childbearing age.

Key Point

Valproic acid should not be used by women with epilepsy who are or wish to become pregnant because of its association with a significantly elevated risk of major congenital malformations and other abnormalities in the fetus.

This patient should begin taking levetiracetam and be weaned off valproic acid. She has juvenile myoclonic epilepsy, which responds particularly well to valproic acid. However, valproic acid should be avoided whenever possible in women of childbearing age because this antiepileptic drug (AED) is associated with a significantly elevated risk (6%-16%) of major congenital malformations, which is much higher than that of other AEDs. In utero exposure to valproic acid also is associated with a 7- to 10-point decrease in intelligence quotient (IQ) on average and an increased risk for autism and autism spectrum disorders in the offspring. Therefore, whenever possible, a trial of another suitable AED should be attempted before pregnancy. This patient should be advised to switch to levetiracetam, which has shown a relatively low risk of birth defects when used in pregnancy. Lamotrigine is another reasonable option, but starting lamotrigine while a patient is still taking valproic acid carries an increased risk of Stevens-Johnson syndrome. If she does not respond to levetiracetam or the drug has adverse effects, lamotrigine, with or without levetiracetam, would be another reasonable choice. If a woman does not respond to treatment with other suitable medications and needs to remain on valproic acid, the dose should be adjusted during pregnancy to the minimum therapeutic dose required. Women should be counseled to use contraception during any period of drug transition from valproic acid because of the drug's significantly increased teratogenic risk.

Carbamazepine is not a good choice for this patient because it is a narrow-spectrum drug used to treat focal epilepsies. Carbamazepine potentially can exacerbate generalized epilepsies, such as juvenile myoclonic epilepsy, and should be avoided in this patient.

Topiramate can be used to treat juvenile myoclonic epilepsy. However, early data suggest that this drug is associated with a moderately increased risk of major congenital abnormalities, particularly cleft lip/cleft palate and small-for-gestational-age infants.

Stopping all AEDs can be considered in some women who have been seizure free for 2 or more years. However, it is rarely an option for patients with juvenile myoclonic epilepsy. These patients typically need life-long AED treatment, and the risk of seizures during pregnancy typically outweighs the potential complications of AED therapy, when selected carefully. The fact that this patient had a seizure after stopping her AED strongly suggests that she should stay on her medication during pregnancy.

Question 53

A 56-year-old woman is evaluated for a 1-year history of tremor. The tremor is more prominent on the right side. She also reports increasing problems with balance and numerous falls, especially when arising from a chair or turning. The patient does not have any significant cognitive symptoms. She has occasional urinary incontinence, intermittent constipation, and a history of acting out of dreams during sleep.

On physical examination, blood pressure is 115/75 mm Hg sitting and 85/70 mm Hg standing, pulse rate is 65/min sitting and 75/min standing, and respiration rate is 22/min. Bruises over the upper and lower extremities secondary to falls are present. On cranial nerve examination, dysmetric saccades, decreased facial expression, and hypophonic speech are noted. Vertical eye movements are normal. A low-amplitude tremor at rest that is more prominent on the right side is present. Repetitive finger tapping movements are bradykinetic. On finger-to-nose testing, mild dysmetria is present. Gait is ataxic with a wide base and frequent veering to both sides; she is unsteady on turning. Gait speed is normal, but arm swing is decreased. A pull test confirms postural instability. No sensory deficits are noted.

Which of the following is the most likely diagnosis?

A
Multiple system atrophy

B
Parkinson disease

C
Progressive supranuclear palsy

D
Vascular parkinsonism

Answer & Critique

Correct Answer: A

Educational Objective: Diagnose a Parkinson-plus syndrome.

Key Point

The combination of parkinsonism, cerebellar ataxia, and early postural instability and falls is most consistent with a diagnosis of multiple system atrophy.

The combination of parkinsonism, cerebellar ataxia, and early postural instability and falls in this patient is most consistent with multiple system atrophy (MSA), a Parkinson-plus syndrome. MSA (Shy-Drager subtype) also can be associated with prominent autonomic deficits, such as orthostatic hypotension and urinary symptoms. Her history of acting out of dreams during sleep (rapid eye movement sleep behavior disorder [RBD]) is another clue suggestive of a synucleinopathy (such as Parkinson disease or MSA). Patients with MSA are at higher risk for falls, dysautonomia, and sleep-related complications, including nocturnal stridor.

Many of this patient's symptoms also can occur in idiopathic Parkinson disease, but her early prominent imbalance, recurrent falls, and cerebellar features are atypical for this disorder.

Progressive supranuclear palsy is the main differential diagnosis, given the patient's early prominent postural instability. She does not, however, have the characteristic impairment in vertical extraocular movements. Additionally, her cerebellar features, asymmetric tremor, hyposmia, and RBD are more typical of multiple system atrophy than progressive supranuclear palsy.

Patients with vascular parkinsonism have sudden or step-wise onset of symptoms and exhibit disproportionate involvement of the lower extremities. The involvement of the upper body, gradual

course, and nonmotor symptoms in this patient make this diagnosis unlikely.

Question 54

A 52-year-old woman is evaluated for a 3-year history of progressively worsening bilateral hand tingling and numbness that are more prominent in the right hand. The numbness involves the thumb and index finger and part of the palm adjacent to the thumb. She says that symptoms are aggravated when she types on a computer keyboard at work, where she is employed as a secretary. She also reports persistent burning and tingling paresthesia over the palmar side of the right thumb and index finger and says she occasionally drops objects with her right hand. The patient has type 2 diabetes mellitus managed by diet and exercise. She takes no medication.

On physical examination, vital signs are normal. Right thumb abductor strength is 4/5; strength in the other muscles of the right hand and right hand grip are normal. Mild atrophy of right thenar eminence in noted. Muscles of the left hand have full strength. Tapping of the right wrist reproduces the symptoms.

Results of nerve conduction studies show ongoing sensorimotor denervation isolated to the right median nerve.

Which of the following is the most appropriate nex t step in management?

A
Decompression surgery

B
Glucocorticoid injection

C
Nocturnal neutral position wrist splint

D
Occupational therapy

Answer & Critique

Correct Answer: A

Educational Objective: Treat carpal tunnel syndrome.

Key Point

Patients with carpal tunnel syndrome who have active denervation on nerve conduction studies and have muscle weakness and atrophy on clinical examination should undergo decompression surgery to prevent irreversible motor weakness.

Decompression surgery is the most appropriate treatment for this patient with carpal tunnel syndrome. Patients with this disorder who have active denervation on nerve conduction studies and have muscle weakness and atrophy on clinical examination should undergo decompression surgery to prevent irreversible motor weakness. Uncontrolled pain and sensory symptoms can be another indication for surgery, but in the absence of motor weakness and active denervation, conservative measures to treat pain and control paresthesia should be attempted first.

Symptomatic treatment, such as NSAIDs, gabapentin, and glucocorticoid injections, and conservative treatment, such as nocturnal neutral position wrist splinting and occupational therapy, may be appropriate therapy for patients with mild to moderate carpal tunnel syndrome, but only if they have no evidence of weakness, atrophy, or active motor denervation on nerve conduction studies. Weight reduction also can be helpful in patients with obesity.

Diabetes mellitus can cause (or predispose one to) compressive mononeuropathies, including median neuropathy at the wrist and ulnar neuropathy at the elbow. However, patients with diabetes who experience hand numbness also should be assessed for carpal tunnel syndrome. The criteria for using surgical decompression to treat carpal tunnel syndrome and the expected response to surgery are similar in patients with and without diabetes.

Question 55

A 58-year-old man is evaluated in the emergency department for a 2-hour history of right-sided weakness. He has hypertension and chronic kidney disease. Medications are amlodipine, lisinopril, and aspirin.

On physical examination, the patient is awake and interactive. Blood pressure is 190/88 mm Hg, pulse rate is 72/min and regular, respiration rate is 16/min, and oxygen saturation is 97% on ambient air. Papilledema is noted. Neurologic examination shows right-sided facial weakness, slurred speech, and absent movement and pinprick sensation in the right arm and leg, but no aphasia.

A CT scan of the head without contrast shows a left thalamic intracerebral hemorrhage.

Results of laboratory studies include a platelet count of 170,000/μL (170×10^9/L), an INR of 0.9, and a serum creatinine level of 1.8 mg/dL (159 μmol/L).

Which of the following is the most appropriate treat ment?

A
Intravenous labetalol

B
Intravenous nitroprusside

C
Platelet transfusion

D
Recombinant factor VIIa

Correct Answer: A

Educational Objective: Treat hypertension after an intracerebral hemorrhage.

Key Point

In patients with intracranial hemorrhage and a systolic blood pressure greater than 180 mm Hg, blood pressure should be lowered to less than 160/90 mm Hg.

This patient should receive labetalol intravenously. He most likely has an intracerebral hemorrhage induced by hypertension. In patients with this type of hemorrhage and a systolic blood pressure greater than 180 mm Hg, acute blood pressure lowering is indicated. Hematoma expansion is a significant source of morbidity and mortality in intracerebral hemorrhage, particularly with extension into the ventricles, and commonly occurs within the first 3 hours after hemorrhage onset. Uncontrolled hypertension is a strong risk factor for hematoma expansion. In this patient, the blood pressure should be lowered to less than 160/90 mm Hg, according to American Heart Association guidelines. A recent clinical trial even reported that lowering blood pressure to less than 140/80 mm Hg was safe and led to a trend in improvement in neurologic outcomes. Labetalol is a fast-acting agent that can be titrated easily.

Intravenous nitroprusside can increase intracranial pressure and thus should be avoided in this patient with a likely intracerebral hemorrhage. The mechanism of action is thought to be related to an increase in cerebral blood volume from either a direct increase in venous volume or impaired venous drainage.

No evidence supports the use of platelet transfusion to improve outcomes in intracerebral hemorrhage or prevent hematoma expansion in patients taking antiplatelet agents. Associated risks of platelet transfusion include transfusion syndrome and volume overload.

Recombinant factor VIIa is inappropriate treatment for this patient. Studies have not shown a beneficial role of hemostatic agents in intracerebral hemorrhage without coagulopathy. In fact, a phase 3 trial that compared recombinant factor VIIa with placebo showed no improvement in neurologic outcomes but a significant increase in the rate of thrombotic complications.

Question 56

A 45-year-old woman is evaluated in the emergency department (ED) 5 minutes after having a witnessed convulsive seizure in the parking lot of the hospital, where she recently started working in the cafeteria. On arrival at the ED, she is obtunded and soon begins to convulse again, exhibiting tonic-clonic movements of both upper extremities. The patient is positioned on her side, and intravenous access is obtained. Medical history cannot be immediately obtained.

On physical examination, temperature is 37.7 °C (99.9 °F), blood pressure is 110/70 mm Hg, pulse rate is 130/min, and oxygen saturation is 93% on ambient air; respiration rate cannot be assessed. This latest seizure has already lasted 6 minutes. Her eyes are open and rolled upward, and the patient is actively convulsing. Initial inspection reveals no evidence of trauma.

Fingerstick blood glucose level is 90 mg/dL (5.0 mmol/L).

Which of the following is the most appropriate intravenous treatment?

A

Diazepam followed by levetiracetam

B

Diazepam followed by phenytoin

C

Lorazepam followed by levetiracetam

D

Lorazepam followed by phenytoin

Answer & Critique

Correct Answer: D

Educational Objective: Treat convulsive status epilepticus.

Key Point

First-line therapy for convulsive status epilepticus is intravenous (IV) lorazepam followed by IV phenytoin or fosphenytoin.

This patient should be treated with intravenous (IV) lorazepam followed by IV phenytoin. She is exhibiting convulsive status epilepticus (CSE), which is defined as convulsive seizures lasting longer than 5 minutes without a return to baseline mental status. CSE is a medical emergency requiring immediate treatment. First-line therapy for CSE is IV lorazepam followed by IV phenytoin or fosphenytoin. This combination has been shown to be superior to a benzodiazepine or phenytoin alone for stopping and providing ongoing control of CSE. When available, fosphenytoin, a prodrug of phenytoin, is preferred over phenytoin because it can be administered faster and does not cause the skin necrosis sometimes seen with phenytoin. Valproic acid also can be used after lorazepam to treat CSE, with several studies showing a similar efficacy to phenytoin. In some patients with known generalized epilepsy syndromes, valproic acid may be a better choice because phenytoin has the potential to provoke absence seizures or absence status epilepticus in these patients.

IV diazepam is less effective that IV lorazepam in treating CSE and thus should not be used if IV lorazepam is available. Rectal diazepam can be used if IV access cannot be obtained. Intramuscular midazolam recently also has been shown to be a good alternative to lorazepam for out-of-hospital CSE or patients without IV access. IV access has been established in this patient.

Levetiracetam has not shown efficacy in the treatment of CSE or been approved by the FDA for use in this clinical scenario. No antiepileptic drugs besides fosphenytoin, phenytoin, and valproic acid are recommended as first-line treatment of CSE.

Question 57

A 49-year-old man is evaluated for persistent sensorimotor symptoms. Five months ago, he developed tingling and mild bilateral pain in the thighs followed by mild weakness and hand numbness. Over the next 3 months, his lower extremity weakness progressively worsened, and his gait became unstable. He began having difficulty going up stairs and opening jars and had several episodes of presyncopal symptoms on standing; his speech, swallowing, and vision were unaffected. His weakness has plateaued within the past 2 months without any improvement. He continues to have tingling in the lower extremities, but the pain has dissipated. The patient has diabetes mellitus treated with metformin. Family history is noncontributory.

On physical examination, blood pressure is 130/75 mm Hg sitting and 95/60 mm Hg standing; other vital signs are normal. Extraocular movements and muscle tone are normal; no fasciculations are present. Diffuse areflexia is noted, with moderate bilateral symmetric weakness in the distal upper extremities and proximal and distal lower extremities. Decreased sensation to pinprick and vibration is noted in both feet; no evidence of high arches or hammertoes is found.

Results of nerve conduction studies show diffuse and severe slowing of motor nerve conduction velocities and the presence of conduction blocks.

Which of the follo wing is the most likely diagnosis?

A

Charcot-Marie-Tooth disease type 1

B

Chronic inflammatory demyelinating polyradiculoneuropathy

C

Diabetic amyotrophy

D

Guillain-Barré syndrome

Answer & Critique

Correct Answer: B

Educational Objective: Diagnose chronic inflammatory demyelinating polyradiculoneuropathy.

Key Point

Progressive weakness, areflexia, and sensorimotor neuropathy with a progression extending beyond 8 weeks since onset of symptoms are characteristic of chronic inflammatory demyelinating polyradiculoneuropathy.

This patient most likely has chronic inflammatory demyelinating polyradiculoneuropathy (CIDP). His rapidly progressive symmetric distal and proximal weakness that plateaued 3 months after onset is consistent with this diagnosis. The diffuse areflexia and sensory and motor neuropathy noted on physical examination and the demyelinating pattern (conduction blocks and slowing of conduction velocities) detected on nerve conduction studies all support the diagnosis of CIDP. CIDP can be idiopathic or associated with a range of systemic conditions, including diabetes mellitus, paraproteinemia, and HIV infection. Recognition of CIDP is essential because the disorder is responsive to glucocorticoids and other forms of immunomodulatory therapy.

Patients with Charcot-Marie-Tooth disease type 1 also have uniform demyelination on nerve conduction studies. However, the clinical course is much slower than in this patient, and symptoms are more prominent in the distal extremities.

Diabetic amyotrophy, also known as proximal lumbosacral radiculoneuropathy, presents with subacute pain and weakness in the proximal lower extremities. The simultaneous involvement of the upper extremities, diffuse areflexia, and diffuse motor nerve abnormalities on nerve conduction studies in this patient are inconsistent with this diagnosis.

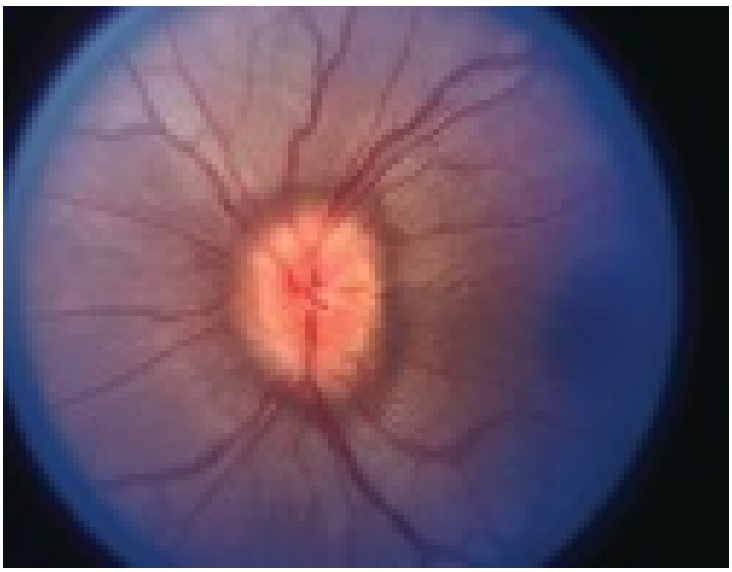
The clinical features of CIDP are very similar to those of Guillain-Barré syndrome, but the latter condition has a faster progression and reaches its nadir within 4 weeks, whereas CIDP progression continues beyond 8 weeks from onset.**Bibliography**

Question 58

A 26-year-old woman is evaluated for progressively worsening headaches that began intermittently 6 months ago and became daily 3 months ago. The patient describes bilateral “vise-like” pain that is steady, moderate in intensity, and unaffected by physical activity. She also has experienced brief, temporal, sharp pains and a few episodes of transient binocular visual dimming. The headaches are accompanied by moderate neck stiffness and mild photophobia but no nausea, phonophobia, or focal neurologic symptoms. She has polycystic ovary syndrome diagnosed 2 years ago and treated with metformin and a combined oral contraceptive but no personal or family history of headache. The patient takes no other medication or supplement.

On physical examination, blood pressure is 124/80 mm Hg and pulse rate is 72/min; BMI is 30. Partial left palsy of the abducens nerve (cranial nerve VI) is noted. A funduscopic photograph is shown.

An MRI is normal. Analysis of cerebrospinal fluid obtained on lumbar puncture shows an opening pressure of 350 mm H_2O.



Which of the following is the most appropriate treatment?

A Acetazolamide
B Amitriptyline
C Epidural blood patch
D Optic nerve sheath fenestration
E Spironolactone

Answer & Critique

Correct Answer: A

Educational Objective: Treat idiopathic intracranial hypertension.

Key Point

Carbonic anhydrase inhibitors, such as acetazolamide, are the only reliably effective medications for idiopathic intracranial hypertension.

The patient should be treated with acetazolamide. Although the headache described has many features of a tension-type headache, the findings of papilledema, partial left palsy of the abducens nerve (cranial nerve VI), and a cerebrospinal fluid (CSF) opening pressure of 350 mm H_2O suggests the presence of a secondary headache syndrome. Documentation of an elevated CSF opening pressure without evidence of a space-occupying lesion on neuroimaging confirms the diagnosis of idiopathic intracranial hypertension (IIH). This condition is most frequently seen in young women with an elevated BMI. The use of a combined oral contraceptive is an additional risk factor. Headache is the most common symptom, and papilledema is the most common physical examination finding. Carbonic anhydrase inhibitors, such as acetazolamide, are the only reliably effective medications for IIH. These inhibitors have been shown to reduce headache and improve visual impairment in patients with IIH.

Amitriptyline is an effective preventive medication for migraine or tension-type headache but would not address this patient's elevated intracranial pressure and thus is inappropriate.

An epidural blood patch is used in the treatment of intracranial hypotension arising spontaneously or occurring after lumbar puncture. This patient has intracranial hypertension.

Optic nerve sheath fenestration involves an incision in the meninges surrounding the optic nerve (cranial nerve II) to relieve elevated intracranial pressure. Optic nerve sheath fenestration can be used in the treatment of IIH but only after the failure of medical management. If acetazolamide does not relieve this patient's symptoms, then optic nerve fenestration may be appropriate.

Spironolactone is a recognized therapy for polycystic ovary syndrome but has no reported effect on headaches or intracranial pressure.

Question 59

A 71-year-old man is seen for follow-up evaluation 2 weeks after having an ischemic stroke. The patient has hypertension and type 2 diabetes mellitus. Medications are enalapril, chlorthalidone, atorvastatin, metformin, and aspirin.

An MRI of the brain obtained during hospitalization showed a right paramedian frontal lobe acute infarction. A magnetic resonance angiogram of the head and neck showed abrupt termination of the distal right anterior cerebral artery but was otherwise normal. An electrocardiogram was normal, and a transthoracic echocardiogram showed a patent foramen ovale, normal systolic and diastolic function, and no valvular disease. Telemetry findings revealed occasional premature atrial contractions.

On current physical examination, vital signs are normal. On neurologic examination, increased tone in the left leg and weakness below the left knee (muscle strength, 4+/5) are noted; the patient ambulates with a cane.

Which of the following is the most appropriate next step in management?

A

Addition of clopidogrel

B

Addition of dabigatran

C

Cardiac rhythm monitoring

D

Percutaneous device closure of the patent foramen oval

Answer & Critique

Correct Answer: C

Educational Objective: Monitor for atrial fibrillation in cryptogenic ischemic stroke.

Key Point

Patients with cryptogenic ischemic stroke require prolonged cardiac monitoring to detect atrial fibrillation, which is found in as many as 25% of these patients.

The most appropriate next step is cardiac rhythm monitoring. The patient has an acute infarction in the anterior cerebral artery territory, which is typically the result of artery-to-artery embolic sources or cardiac embolism. This diagnosis is supported by the abrupt termination of the artery seen on magnetic resonance angiography. Until final stroke classification can be confirmed, the patient has a cryptogenic stroke. The patient's vascular imaging did not show extracranial or intracranial internal carotid artery stenosis, which makes cardiac embolism more likely. In several reports, as many as 25% of patients with cryptogenic ischemic stroke have paroxysmal atrial fibrillation on prolonged cardiac monitoring of up to 30 days; patients who have premature atrial contractions and other findings of ectopy on short-term telemetry may be more likely to have this finding. Continued cardiac rhythm monitoring to detect atrial fibrillation is thus advisable in this patient.

Clopidogrel should not be added to this patient's medication regimen because the combination of aspirin and clopidogrel was associated with an increased risk of major hemorrhage without any associated clinical benefit in several clinical trials in the subacute setting.

Dabigatran and other novel anticoagulants have only been approved for stroke prevention in the setting of atrial fibrillation, which has not yet been diagnosed in this patient.

Patent foramen ovale (PFO) closure did not reduce the risk of ischemic stroke more than best medical therapy in patients with cryptogenic stroke in the recently completed CLOSURE I trial. The risk of recurrent stroke in patients with an otherwise isolated PFO, with or without an atrial septal aneurysm, is low in most clinical trials. In older patients, a PFO frequently is an incidental finding and unlikely to be causally related to the infarct.

Question 60

A 68-year-old man is seen for follow-up evaluation of Parkinson disease, which was diagnosed 10 years ago. Although his symptoms initially were well controlled with medications, he has experienced increasing fluctuations in motor symptoms, specifically tremor at rest and slowness, within the past 3 years. Medications are carbidopa-levodopa, entacapone, and amantadine. He notes marked symptom improvement after taking these medications, but the benefit lasts only for 2 hours. Increased dosing of carbidopa-levodopa causes visual hallucinations.

On physical examination performed 3 hours after the patient took carbidopa-levodopa, blood pressure is 130/65 mm Hg and pulse rate is 85/min. Masked facies, an asymmetric upper extremity tremor at rest, marked bradykinesia, and cogwheel rigidity are noted. Gait is slow, but cognitive assessment findings are normal. Repeat examination performed 1 hour after the patient took carbidopa-levodopa reveals notable improvement in bradykinesia, rigidity, and gait and the emergence of prominent dyskinesia.

Which of the following is the most appropriate treatment of this patient's motor complications?

A

Deep brain stimulation

B

Discontinuation of entacapone

C

Increased amantadine dosage

D

Ropinirole

E

Selegiline

Answer & Critique

Correct Answer: A

Educational Objective: Treat advanced Parkinson disease with motor complications.

Key Point

Deep brain stimulation is the appropriate treatment of patients with advanced Parkinson disease who continue to benefit from dopaminergic medications but experience medication-related complications.

Deep brain stimulation is the appropriate treatment of this patient with advanced Parkinson disease who continues to benefit from dopaminergic medications but experiences medication-related complications. His initial marked benefit from carbidopa-levodopa wears off before he takes the next dosage. Appropriate initial steps to alleviate this problem included increasing the frequency of carbidopa-levodopa dosing and adding entacapone to prolong the effect of the carbidopa-levodopa after it is taken. However, he developed prominent medication-induced dyskinesia and visual hallucinations, which both limit further medical management. Deep brain stimulation of the subthalamic nucleus is likely to provide more sustained control of his medication-responsive motor deficits and allow a reduction in his medications; this, in turn, should resolve any medication-induced hallucinations or dyskinesia.

Discontinuing entacapone is likely to diminish the patient's dyskinesia but at the same time would remove the beneficial effect of prolonging the action of the carbidopa-levodopa and thus lead to earlier wearing off of its benefit.

Although amantadine can be effective against dyskinesia, increasing the dosage further may worsen the hallucinations.

Adding a dopamine agonist, such as ropinirole, may boost the dopaminergic effect of the carbidopa-levodopa, but this medication also is likely to worsen the patient's hallucinations and dyskinesia and should be avoided.

Adding a monoamine oxidase B inhibitor, such as selegiline, also is likely to worsen his dyskinesia and thus is inappropriate.

Question 61

An 84-year-old woman is evaluated for rapidly increasing confusion and behavioral problems. Alzheimer disease was diagnosed 2 years ago, and she was started on donepezil at that time; symptoms have slowly progressed since diagnosis. Her husband, who is her caregiver, reports that 5 days ago, she began having greater difficulty locating the bathroom in their home, has not recognized members of her immediate family on several occasions, has experienced greater nighttime confusion, has become verbally abusive, and has frequently attempted to leave the house unaccompanied. The patient also has hypertension. Medications are donepezil and enalapril.

On physical examination, temperature is 37.2 °C (99.0 °F), blood pressure is 110/70 mm Hg, pulse rate is 84/min and regular, respiration rate is 14/min, and oxygen saturation is 99% on ambient air. Neurologic examination shows a drowsy but easily arousable patient who is oriented to neither time nor place. Her attention is poor, and she has difficulty following even simple commands. Other physical examination findings are unremarkable.

Which of the following is the most appropriate next step in management?

A

Add quetiapine

B

Discontinue donepezil

C

Evaluate for concurrent illness

D

Order head CT

Answer & Critique

Correct Answer: C

Educational Objective: Identify the cause of delirium in a patient with dementia.

Key Point

Underlying cognitive impairment or dementia is a significant risk factor for delirium; identification of any concurrent illness(es) causing the delirium should be the first step in management.

This patient should undergo testing for concurrent illnesses. She has had an acute change in cognitive symptoms accompanied by fluctuating symptoms, inattention, and a depressed level of consciousness. This presentation is consistent with delirium, which should be recognized early and treated by correction of the underlying cause. Underlying cognitive impairment or dementia is a significant risk factor for delirium. The acute change in mental status experienced by this patient is unlikely to be due to worsening dementia, given that the disease course has been slowly progressive to this point. Features of inattention and a depressed level of arousal are not common in Alzheimer disease until late in the disease course. The initial evaluation should focus on ruling out the most common metabolic and infectious causes of delirium in older patients by obtaining a complete blood count, serum electrolyte and plasma glucose levels, liver chemistry and kidney function tests, urinalysis, and a chest radiograph. Additional tests should be tailored to the clinical presentation.

Initiation of quetiapine is premature in this patient. Immediate therapy should focus on identifying and treating the underlying cause of delirium. For agitation, nonpharmacologic interventions should be tried first, such as frequent reorientation, avoiding immobilization and catheterization, restoring normal sleep patterns, and minimizing disruptions in the environment. Only if these steps prove inadequate should treatment with dopamine antagonists be considered.

Although cholinesterase inhibitors, such as donepezil, may be associated with cholinergic adverse effects in some patients, these effects tend to occur shortly after starting the medication or increasing the dose. This patient has tolerated a stable dose of donepezil for at least 1 year, and so it would not be appropriate to attribute her acute delirium to this medication. Evaluation for another cause should be pursued.

Neuroimaging is not indicated in the immediate evaluation of this patient because the findings on neurologic examination were nonfocal. If the initial testing for concurrent illnesses is unrevealing, additional evaluation would include neuroimaging to rule out hemorrhage, territorial infarction, or mass lesion.

Question 62

A 49-year-old man has a follow-up evaluation 3 months after an exacerbation of multiple sclerosis (MS) that resulted in bilateral leg weakness. He has had MS for 15 years. The patient reports that for the past 10 weeks, he has had bilateral muscle cramps in the thighs and calves and frequent nighttime episodes of right leg stiffening and spasms that can last from seconds to hours and impair his sleep. He has no other symptoms and no significant family history. Medications are fingolimod and vitamin D supplements.

On physical examination, temperature is 36.4 °C (97.5 °F), blood pressure is 130/50 mm Hg, and pulse rate is 88/min. Increased tone is noted in both legs. Palpation of the leg muscles elicits no pain or fasciculations. Muscle strength is 4/5 in both legs. Patellar and ankle reflexes are 3+. An extensor plantar response is noted on the right. Gait requires the assistance of a cane, and both legs appear stiff when walking.

Results of laboratory studies show a normal serum creatine kinase level.

Which of the following is the most appropriate management?

A

Electroencephalography

B

Electromyography

C

Oral baclofen

D Oral pramipexole

Answer & Critique

Correct Answer: C

Educational Objective: Treat multiple sclerosis–related spasticity.

Key Point

Baclofen is appropriate for treatment of muscle spasms and cramps due to corticospinal tract injury from multiple sclerosis.

This patient should be treated with a skeletal muscle relaxant, such as oral baclofen. He is experiencing muscle spasms and cramps as a long-term consequence of corticospinal tract injury from multiple sclerosis. Damage to upper motoneuron pathways has resulted in reduced inhibition of reflex arcs in the spinal cord, which allows for tonic activation of the lower motoneuron and resultant spasms and cramps. These symptoms can be reduced with the use of skeletal muscle relaxant medications, including baclofen, tizanidine, and cyclobenzaprine. Some patients may require intrathecal baclofen pumps or botulinum toxin injections for refractory symptoms.

Electroencephalography would be an appropriate test if a high suspicion of seizure was present. This patient's history and clinical evaluation do not suggest seizure, and his symptoms are highly consistent with upper motoneuron spasticity.

Because the physical examination findings are clearly consistent with an upper motoneuron injury, electromyography (EMG) (nerve conduction studies and needle electrode examination) is inappropriate. EMG is most appropriate for disorders of the lower motoneuron, neuromuscular junction, or muscle. The lack of fasciculations makes lower motoneuron injury even less likely, and the normal serum creatine kinase level and lack of pain on muscle palpation make an inflammatory myopathy very unlikely.

Pramipexole would be an appropriate treatment for restless legs syndrome (RLS), but this patient is not experiencing RLS symptoms. RLS does not result in upper motoneuron signs on examination or daytime muscle cramps. Also, patients with RLS experience feelings of discomfort in the legs or periodic limb movements while sleeping, not tonic leg spasms and cramps as with this patient.

Question 63

A 24-year-old woman is seen for a follow-up evaluation of epilepsy first diagnosed 4 years ago. The patient has five or six simple or complex partial seizures annually that have been difficult to control. The epilepsy was first treated with lamotrigine, to which levetiracetam was added 2 years ago. Although both medications decreased the frequency and intensity of the seizures when initiated, the episodes returned to their former state after several months. She cannot drive because the seizures often cause loss of consciousness. She has a history of febrile seizure as an infant. She otherwise has no significant medical history, and her only medications are lamotrigine, levetiracetam, and folic acid.

All physical examination findings are within normal limits.

An MRI shows right mesial temporal sclerosis. Video electroencephalographic monitoring records three complex partial seizures, all originating from the right temporal lobe, and interictal right anterior temporal sharp waves.

Which of the following is the most effective treatment?

21%

A

Addition of carbamazepine

5%

B

Ketogenic diet

65%

C

Right temporal lobectomy

10%

D

Vagal nerve stimulation

]Answer & Critique

Correct Answer: C

Educational Objective: Treat refractory temporal lobe epilepsy.

Key Point

In patients with refractory temporal lobe epilepsy, surgery is the most likely intervention to stop seizures and thus improve quality of life.

Right temporal lobectomy is the intervention most likely to make this patient seizure free and thus improve her quality of life. She has refractory epilepsy, defined as the persistence of disabling seizures for longer than 1 year despite treatment with adequate doses of two or more antiepileptic drugs (AEDs). Surgery is the most likely intervention to stop the seizures, and seizure freedom is closely tied to quality of life in a patient with refractory epilepsy. Given her history of febrile seizures in infancy and the presence of mesial temporal sclerosis on the MRI, her chances of seizure freedom 2 years after surgery are at least 70%.

Patients who do not respond to either their first or their second AED (in sequence or conjunction) have a less than 10% chance of experiencing seizure remission with pharmacotherapy. Therefore, adding a third agent, such as carbamazepine, to her medication regimen is unlikely to stop the seizures or improve her quality of life. Although carbamazepine could be offered in an attempt to temporize the situation while she awaits a surgical evaluation, it would not be the most effective management.

The ketogenic diet and vagal nerve stimulation are palliative treatments that can lessen the seizure burden in patients who are not candidates for epilepsy surgery. Both options rarely lead to seizure freedom.

Question 64

A 66-year-old man is evaluated in the hospital 3 days after fracturing his hip in a fall. He underwent surgical repair 1 day after admission and had an unremarkable initial postoperative course but now is confused and agitated. Medical history includes anxiety disorder and a 10-year history of Parkinson disease. Medications before hospitalization were levodopa, amantadine, and citalopram. All medications have been withheld since admission.

On physical examination, temperature is 39.5 °C (103.1 °F), blood pressure is 168/80 mm Hg (baseline, 118/70 mm Hg), pulse rate is 90/min, and respiration rate is 28/min. The patient appears rigid, does not follow commands, and is agitated. Deep tendon reflexes are normal, but muscle tone is markedly increased. A resting tremor is present bilaterally but is more pronounced on the right side. No spontaneous or stimulus-induced myoclonus is noted. Dystonic posturing is noted in the right foot.

In addition to continuing supportive care, which of the following is the most appropriate treatment?

A

Administer baclofen

B

Administer dantrolene

C

Restart citalopram

D

Restart levodopa

Answer & Critique

Correct Answer: D

Educational Objective: Treat parkinsonian-hyperpyrexia syndrome secondary to dopaminergic medication withdrawal.

Key Point

In hospitalized patients with Parkinson disease, sudden withdrawal of dopaminergic medications can lead to parkinsonian-hyperpyrexia syndrome, an acute syndrome resembling neuroleptic malignant syndrome; restarting the medications is the mainstay of therapy.

Levodopa should be restarted in this patient. Sudden withdrawal from dopaminergic medications, as may occur during hospitalization in patients with Parkinson disease, can lead to an acute dopamine agonist withdrawal syndrome, termed parkinsonian-hyperpyrexia syndrome, which resembles neuroleptic malignant syndrome (NMS). Patients who abruptly stop taking dopaminergic medications can develop acute altered mental status, hyperthermia, rhabdomyolysis, and extrapyramidal symptoms, including severe rigidity and dystonia. A high index of suspicion for parkinsonian-hyperpyrexia syndrome is required in these patients because mortality rates of up to 4% have been reported and may be prevented by early recognition and treatment. The differential diagnosis also includes central nervous system infection and status epilepticus. Aggressive supportive care, which may include intensive care and respiratory support, is appropriate. The primary medical therapy is restoration of dopaminergic medication.

Administration of the skeletal muscle relaxant baclofen may be helpful in patients with severe spasticity or progressive encephalomyelitis with rigidity and myoclonus, but not in those with Parkinson disease or disorders due to withdrawal from dopaminergic medications.

Dantrolene is a skeletal muscle relaxant that has proven efficacy in treating malignant hyperthermia and NMS. However, its effectiveness in parkinsonian-hyperpyrexia syndrome has not been established.

The clinical manifestations of serotonin syndrome may overlap with those of parkinsonian-hyperpyrexia syndrome and NMS, although serotonin syndrome is more often associated with hyperreflexia and myoclonus and not extrapyramidal symptoms. It typically occurs in patients

taking high doses of serotoninergic agents (such as citalopram) and would not be expected in this patient in whom this medication has been withheld. Restarting the citalopram would not address the underlying disease process in this patient.

Question 65

A 23-year-old woman is evaluated in the hospital for a 3-day history of a severe right hemicranial headache that has not responded to medication. She has had recurrent migraine for 17 years that typically involves severe right hemicranial throbbing pain associated with nausea and vomiting. Once or twice annually, the headaches are preceded by visual aura. Since age 13 years, migraine attacks have occurred twice monthly, with menses and ovulation as triggers. Typical duration is 24 hours, although occasionally episodes linger for 4 to 5 days. The patient also has anxiety. Medications are zolmitriptan for acute treatment of headache and alprazolam for anxiety. An infusion of fluids, intravenous prochlorperazine, and ketorolac in the emergency department brought no relief of symptoms.

On physical examination, blood pressure is 108/68 mm Hg and pulse rate is 86/min. All other physical examination findings, including those from a neurologic examination, are normal.

Which of the following is the most appropriate next step in management?

A Brain MRI

B Combined oral contraceptives

C Dihydroergotamine

D Hydromorphone

E

Sertraline

Answer & Critique

Correct Answer: C

Educational Objective: Treat status migrainosus.

Key Point

Repetitive administration of intravenous dihydroergotamine is the most appropriate in-patient treatment of status migrainosus.

The patient has status migrainosus and should receive repetitive intravenous infusions of dihydroergotamine. Status migrainosus is defined as a migraine attack extending beyond 72 hours and is the most common complication of acute migraine. The condition is characterized by persistent severe pain that often is accompanied by protracted nausea with vomiting and profound sensory sensitivities. Hormonal factors are extremely common as inciting events. Life stressors, mood or anxiety disorders, and acute medication overuse may be other contributing factors. Triptans are often unsuccessful in resolving a migraine of this duration, but parenteral hydration and antiemetic medications sometimes provide some relief. Because this patient has not responded to either of these treatments or to the ketorolac administered in the emergency department, the next step is repetitive administration of intravenous dihydroergotamine. This drug is administered in conjunction with either prochlorperazine or metoclopramide over the course of 1 to 3 days. Outpatient treatment options include a several-day course of oral glucocorticoids.

The patient has normal findings on neurologic examination. An MRI of the brain is unlikely to provide any additional useful information.

Combined oral contraceptives should be avoided in patients with migraine with aura because they further increase stroke risk, which is already elevated in this patient.

Opioids, such as hydromorphone, may provide analgesia but often contribute to worsening migraine frequency or intensity. They should be avoided in patients with acute migraine when other options are available.

Sertraline may help control anxiety but contributes nothing to the acute or preventive treatment of migraine and thus is inappropriate for this patient.

Question 66

A 29-year-old woman is evaluated during a routine follow-up examination of multiple sclerosis, which was diagnosed 3 years ago. The patient says she wishes to discontinue her oral contraceptive and attempt to become pregnant. She has no other personal or family medical history of note. Medications are fingolimod, vitamin D, and an oral contraceptive.

On physical examination, temperature is 36.9 °C (98.5 °F), blood pressure is 100/50 mm Hg, pulse rate is 66/min, and respiration rate is 14/min; BMI is 27. A right afferent pupillary defect is noted. All other physical examination findings are normal.

Besides discontinuing the oral contraceptive, which of the following is the most appropriate next step in management?

A

Advise against pregnancy

B

Discontinue fingolimod

C

Substitute mitoxantrone for fingolimod

D

Substitute teriflunomide for fingolimod

Answer & Critique

Correct Answer: B

Educational Objective: Modify pharmacologic therapy for multiple sclerosis in the setting of pregnancy.

Key Point

Fingolimod is classified as a pregnancy category C drug (safety in human pregnancy not clearly established) and thus should not be used by women who are pregnant or planning to become pregnant.

In addition to discontinuing the oral contraceptive in preparation for attempting conception, fingolimod should be stopped. An oral disease-modifying therapy for multiple sclerosis (MS), fingolimod is a sphingosine-1-phosphate receptor modulator that restricts activated lymphocytes to lymph nodes and may also have direct neuroprotective effects. Fingolimod significantly reduces the relapse rate, risk of disability progression, and accumulation of new lesions on MRI. This drug has been associated with rare but potentially harmful side effects, including increased rates of serious herpesvirus infection, hypertension, bradycardia, lymphopenia, liver function abnormalities, and macular edema. Fingolimod is classified as a pregnancy category C drug, and thus its safety in human pregnancy is not clearly established. Although category C medications are indicated in some patients if the benefits outweigh the risks, the hormonal state of pregnancy itself is protective against MS activity, and thus discontinuing a disease-modifying drug during pregnancy is considered relatively safe.

Advising this patient against pregnancy is clearly inappropriate. The adverse effect of pregnancy on MS progression is a commonly held misconception. In fact, observational studies have found reduced risks for conversion to clinically definite MS from clinically isolated syndromes and reduced risks for conversion from relapsing MS to secondary progressive MS in women with multiple pregnancies.

Mitoxantrone is an anthracenedione chemotherapeutic agent that reduces lymphocyte proliferation and decreases the relapse rate and disability progression in MS. Despite mitoxantrone's efficacy, cardiac toxicity and the risk of secondary leukemia have significantly limited its use. Mitoxantrone is classified as a pregnancy category X drug and is contraindicated during pregnancy.

The MS drug teriflunomide is the active metabolite of leflunomide, which inhibits pyrimidine biosynthesis and interferes with the interaction between T lymphocytes and antigen-presenting cells. Substituting teriflunomide for fingolimod is inappropriate because teriflunomide is classified as pregnancy category X drug and is contraindicated during pregnancy.

Question 67

A 37-year-old woman is admitted to the ICU after a CT scan of the head without contrast obtained in the emergency department showed a thin, diffuse subarachnoid hemorrhage without hydrocephalus or cerebral edema and a subsequent angiogram revealed a 10-mm anterior communicating artery aneurysm. The patient is treated with a coiling procedure without complications.

One day after the procedure, physical examination shows a blood pressure of 134/68 mm Hg, a pulse rate of 96/min, and a respiration rate of 12/min. Nuchal rigidity is noted. The patient has difficulty remaining awake unless spoken to loudly, but no other abnormalities are seen on neurologic examination.

A transcranial ultrasound obtained the same day is normal. Fingerstick blood glucose readings over the next 24 hours range between 120 and 150 mg/dL (6.7-8.3 mmol/L).

Which of the following is the most appropriate nex t step in treatment?

A

Intravenous dopamine

B

Intravenous insulin

C

Oral nimodipine

D

Oral simvastatin

Answer & Critique

Correct Answer: C

Educational Objective: Prevent neurologic complications with nimodipine after subarachnoid hemorrhage.

Key Point

Oral nimodipine is indicated in all patients with aneurysmal subarachnoid hemorrhage.

This patient should receive oral nimodipine. Nimodipine is an L-type calcium channel blocker that has reduced the incidence of vasospasm in clinical trials involving patients with subarachnoid hemorrhage; morbidity and mortality also were reduced, even among patients who did not have cerebral vasospasm. Nimodipine may improve outcomes by preventing vasospasm and by a neuroprotective mechanism, particularly because calcium influx into neurons is a common pathway of cell injury in ischemia. Administration of oral nimodipine for 21 days after the hemorrhage is indicated in all patients with aneurysmal subarachnoid hemorrhage. This patient had an aneurysmal subarachnoid hemorrhage that was appropriately treated. In the first 48 hours after subarachnoid hemorrhage, rebleeding and hydrocephalus can cause neurologic worsening that is associated with significant morbidity and mortality.

Because the patient has no evidence of cerebral artery vasospasm, such as deterioration in level of consciousness or new focal neurologic deficits, treatment with intravenous dopamine is inappropriate. Vasospasm with subsequent cerebral ischemia is a significant contributor to neurologic worsening and poor long-term outcomes in patients with aneurysmal hemorrhage. Patients with a thick clot in the base of the brain are at higher risk of vasospasm, which can be detected before symptom onset on a transcranial Doppler ultrasound. This patient, however, has no clinical, objective, or imaging signs of vasospasm that would warrant prophylactic treatment with a vasopressor.

Intravenous insulin should not be given to this patient. Her blood glucose levels are mildly elevated, but acute management of mild hyperglycemia has not shown benefit in patients with all stroke subtypes. Because of the risk of hypoglycemia, the American College of Physicians (ACP) and other organizations recommend not using intensive insulin therapy to normalize blood glucose

levels in critically ill patients with or without diabetes mellitus. If insulin therapy is required, the ACP recommends target blood glucose levels of 140 mg/dL to 200 mg/dL (7.8-11.1 mmol/L).

The efficacy of statins for secondary stroke prevention or as a neuroprotective agent in subarachnoid hemorrhage has not been established. Statins are indicated for secondary stroke prevention in patients with ischemic stroke or transient ischemic attack of a presumed atherosclerotic subtype.

Question 68

A 29-year-old woman is seen for a routine follow-up evaluation. Multiple sclerosis (MS) was diagnosed 2 months ago. She has no current symptoms. The patient does not smoke, drinks a glass of wine with dinner three or four times weekly, and exercises at least 3 hours weekly. Her father has hypertension, but she has no other significant family history. Daily medications are glatiramer acetate, a multivitamin, and a calcium–vitamin D supplement.

On physical examination, temperature is 37.3 °C (99.1 °F), blood pressure is 108/48 mm Hg, pulse rate is 62/min, and respiration rate is 12/min; BMI is 20. All other physical examination findings, including those from a neurologic examination, are normal.

Which of the following is the most appropriate preventive or screening strategy f or this patient?

A

Alcohol cessation

B

Annual influenza vaccination

C

Urinalysis

D Use of an oral contraceptive

Answer & Critique

Correct Answer: B

Educational Objective: Provide preventive therapy in multiple sclerosis.

Key Point

Routine vaccinations, such as an annual influenza vaccination, are recommended for patients with multiple sclerosis (MS) to prevent infections leading to a heightened immune state and potential MS relapse.

This patient should have a yearly influenza vaccination. She takes the disease-modifying drug glatiramer acetate, a pregnancy category B drug, for her multiple sclerosis (MS). The patient already exercises at least 3 hours weekly, takes a daily calcium–vitamin D supplement, and does not smoke, all recommended preventive measures against osteoporosis or conversion to secondary progression in patients with MS. According to a position statement by the American Academy of Neurology, there is no evidence of adverse outcomes of routine vaccinations in patients with MS beyond what is expected in the general population. In fact, these vaccinations are recommended to prevent infections leading to a heightened immune state and potential MS relapse.

Moderate alcohol usage has not been shown to adversely affect MS outcomes and has no effect on the metabolism of glatiramer acetate. Therefore, alcohol cessation is not necessary.

Although urinary tract infections (UTIs) are more common among patients with MS because of neurogenic bladder dysfunction, screening urinalysis is not indicated as a preventive medicine strategy in this patient population, barring UTI symptoms.

Despite the commonly held belief that pregnancy results in adverse events in MS, all evidence points instead toward to the protective effect of the hormonal state of pregnancy. Multiparous women with MS have equivalent, or perhaps better, outcomes than women with MS who have never been pregnant. Initiating an oral contraceptive is indicated only if the patient wishes to avoid pregnancy, but not as a preventive strategy for worsening of MS.

Question 69

A 35-year-old man is evaluated for recurrent headaches. For the past 5 years, he has had weekly episodes of headache lasting 6 to 8 hours. The patient describes the pain as a steady pressure affecting the frontal and maxillary regions that is exacerbated by physical activity. When severe, the pain radiates to the temples and occiput. He also experiences nasal congestion and sensitivity to light, noise, and odors with the headaches but has had no gastrointestinal or other neurologic symptoms. Potential headache triggers include drastic weather changes, strong odors, and stress. The patient also has allergic rhinitis. Medications are acetaminophen and fexofenadine, which have been ineffective in relieving the headaches and their associated symptoms.

On physical examination, blood pressure is 114/72 mm Hg and pulse rate is 66/min. Other physical examination findings, including those from a neurologic examination, are normal.

Which of the following is the most appropriate next step in management?

A

CT of the head

B

CT of the sinuses

C

Naproxen

D

Pseudoephedrine

E

Sumatrip

Answer & Critique

Correct Answer: C

Educational Objective: Treat migraine without aura with an NSAID.

Key Point

Evidence-based guidelines suggest that NSAIDs, triptans, and dihydroergotamine are effective treatments for acute migraine without aura and that NSAIDs are preferred as initial treatment because of their greater cost-effectiveness.

The patient should receive naproxen to treat his headaches, which meet criteria for migraine without aura. Episodes of migraine without aura typically last between 4 and 72 hours if untreated. Two of four pain features are necessary for the diagnosis to be made: unilateral location, throbbing quality, moderate to severe intensity, and worsening with physical activity. Either nausea or a combination of photophobia and phonophobia also is required. Patients with this diagnosis commonly report sinus pressure or drainage with these episodes, which often leads to the incorrect diagnosis of sinus headache. Common triggers include stress, hormonal or weather changes, alterations in sleep or meal patterns, or strong light, noise, or odor stimuli. Neurologic examination findings are normal. Evidence-based guidelines suggest that NSAIDs (such as naproxen), triptans, and dihydroergotamine are effective therapy for this type of acute migraine but that NSAIDs are preferred as initial treatment because of their greater cost-effectiveness.

In the context of a stable pattern of headaches that meets the criteria for migraine, CT of the head in unnecessary. Similarly, the headache pattern described by this patient—weekly headache episodes lasting 6 to 8 hours—is incompatible with an acute or chronic sinus pathology, which makes CT of the sinuses also unlikely to add any useful information.

Pseudoephedrine is effective in alleviating sinus congestion but has no role in the treatment of migraine. Headache is a relatively late-appearing and minor symptom of acute sinusitis; major symptoms include facial pain, purulent discharge, fever, and hyposmia, none of which this patient reports.

Question 70

A 48-year-old man is evaluated for right upper extremity weakness. For the past 8 months, he has noticed progressive weakness in the right arm that is more prominent in the fingers; proximal strength is preserved. He also has noted frequent, painful muscle cramping in the right arm, lower back, and left lower extremity that recently has been accompanied by muscle twitching. He has had no sensory deficit or significant medical history. The patient takes no medication.

On physical examination, vital signs are normal. The patient's speech is dysarthric. Muscle strength testing shows weakness with atrophy in the distal right upper extremity and mild weakness without atrophy in the left lower extremity. Fasciculations are present in the bilateral upper and lower extremities and the paraspinal muscles. Deep tendon reflexes are brisk in all extremities, and the plantar response is extensor. Results of sensory and motor examinations are normal.

Results of laboratory studies—including a complete metabolic profile; serum lead, copper, vitamin B_{12}, and parathyroid hormone levels; and Lyme antibody titers—are unremarkable.

MRIs of the cervical and lumbar spines are normal. Results of needle electrode examination show evidence of lower motoneuron abnormalities in multiple body regions, including the limbs, trunk, and face.

Which of the following is the most appropriate treatment?

A

Bilevel positive airway pressure

B

Intravenous immune globulin

C

Percutaneous endoscopic gastrostomy

D

Riluzole

Answer & Critique

Correct Answer: D

Educational Objective: Treat amyotrophic lateral sclerosis with riluzole.

Key Point

Riluzole, the only FDA-approved medication for amyotrophic lateral sclerosis, can increase the survival of affected patients by an average of 3 months

This patient should receive riluzole. Clinical and electromyographic evidence of simultaneous upper and lower motoneuron signs in multiple body regions is most consistent with a diagnosis of amyotrophic lateral sclerosis (ALS). Onset in a single limb, rapid progression, bulbar involvement, and MRI evidence of a corticospinal tract abnormality further support the diagnosis, which was confirmed by results of the needle electrode examination. The absence of an alternative likely cause of his symptoms, such as Lyme disease, hyperparathyroidism, vitamin B_{12} or copper deficiency, lead intoxication, or combined cervical myelopathy and neuropathy, also suggests the diagnosis.

Riluzole is the only FDA-approved medication for ALS and can increase the survival of affected patients by a modest average of 3 months. It should be offered to all patients with a new diagnosis of ALS who wish to maximize their survival.

Bilevel positive airway pressure and other similarly noninvasive respiratory support methods can increase survival in ALS and should be started in the presence of respiratory symptoms and hypercarbia, which are absent in this patient.

Although intravenous immune globulin (IVIG) can be used in the management of chronic inflammatory demyelinating polyradiculoneuropathy (CIDP), this patient's clinical history and findings on needle electrode examination, especially the prominent upper motoneuron signs and absence of sensory deficits, are inconsistent with CIDP. IVIG is not indicated for the management of ALS.Percutaneous endoscopic gastrostomy should be considered in patients with ALS and dysphagia before they reach the advanced stages of the disease to improve nutrition and increase survival. This intervention would be premature in this patient, however, who has no signs of dysphagia.

Question 71

A 59-year-old woman is evaluated for headaches and occasional double vision. The patient has had episodes of migraine with aura since age 12 years. Aura symptoms include visual blurring and ipsilateral facial numbness lasting approximately 15 minutes. After menopause, migraine attacks became less frequent and intense, declining from 12 to 5 days per month, but over the past 4 months have again become more frequent, increasing to 15 days per month. She describes these recent headaches, which are not associated with her typical aura, as more bilateral and “squeezing” in nature than previous ones and reports intermittent visual blurring and two instances of horizontal diplopia lasting 2 hours. The patient has had no other neurologic symptoms. The recent headaches respond to neither ibuprofen nor to the naratriptan she uses to treat acute migraine episodes. Her only other medication is amitriptyline for migraine prophylaxis.

On physical examination, blood pressure is 128/86 mm Hg and pulse rate is 78/min; BMI is 27. Other results of the general medical and neurologic examinations are normal.

Which of the following is the most a ppropriate management?

75%

A

Brain MRI

10%

B

Discontinuation of ibuprofen

3%

C

Lumbar puncture

4%

D

Substitution of sumatriptan for naratriptan

9%

E

Substitution of topiramate for amitriptyline

Answer & Critique

Correct Answer: A

Educational Objective: Diagnose a secondary headache.

Key Point

Recent escalation of headache frequency in patients with migraine suggests a secondary headache disorder and should be evaluated with brain MRI.

The patient should undergo brain MRI. Although she has a long-standing history of migraine with aura, the recent escalation in headache frequency and intensity is concerning. The pattern of her headaches has fundamentally changed, and she exhibits several other red flags, such as the development of a new headache condition after age 50 years and neurologic symptoms lasting more than 1 hour, that are compatible with the presence of a secondary headache. Diplopia, when present in migraine aura, should be accompanied by other features seen in migraine with brainstem aura (basilar migraine), such as vertigo, ataxia, dysarthria, diplopia, tinnitus, hyperacusis, or alteration in consciousness; this patient has none of these features. Additionally, the maximum duration of aura in basilar migraine is 60 minutes or less, not the 2 hours she experienced. MRI is the preferred study to confirm the diagnosis of a secondary headache.

Discontinuation of ibuprofen would be helpful in the setting of medication overuse headache. Excessive analgesic intake can result in worsening of the underlying headache or the appearance of a milder, nonspecific headache. However, this medication would not cause new neurologic symptoms, such as diplopia.

In this patient with a probable secondary headache, neuroimaging is necessary before consideration of lumbar puncture to exclude any space-occupying lesion that could affect intracranial pressure.

Switching from naratriptan to sumatriptan may have been a consideration if the diagnosis were only worsening migraine. However, this patient most likely has a secondary headache disorder, so changing triptans in unlikely to be helpful.

Substituting topiramate for amitriptyline may be an appropriate treatment in patients with escalating migraine frequency, but not in those suspected to have a secondary headache disorder.

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Question 72

A 46-year-old woman is evaluated for intermittent left-sided tingling and a subsequent headache. She was seen in an emergency department 3 weeks ago for similar symptoms. At that time, a noncontrast CT scan of the head and an MRI of the brain were normal, but a magnetic resonance angiogram showed a 5-mm left middle cerebral artery aneurysm. Results of cerebrospinal fluid analysis were normal. The patient has hypertension and migraine, but she has no other medical history of note. She has a 15-pack-year smoking history, currently smoking approximately ten cigarettes daily, and does not drink alcoholic beverages. Her only medication is amlodipine.

On physical examination, vital signs are normal. Other results of the general and neurologic examinations are normal.

Which of the following is the most appropriate next step?

A

Aneurysmal clipping

B

Endovascular coiling

C

Smoking cessation counseling

D

Substitution of nimodipine for amlod

Answer & Critique

Correct Answer: C

Educational Objective: Counsel a patient with an unruptured cerebral aneurysm about smoking cessation.

Key Point

Patients with unruptured intracranial aneurysms should be counseled to stop smoking because of the increased risk of aneurysmal rupture.

This patient should be counseled about smoking cessation and provided with smoking cessation aids as appropriate, including nicotine replacement or pharmacologic treatment. She has an unruptured intracranial aneurysm of the left middle cerebral artery. A subarachnoid hemorrhage (SAH) has been ruled out by neuroimaging and lumbar puncture findings. She has no history of a previous SAH, and the aneurysm measures less than 7 mm, both of which indicate a low risk of rupture. The major risk factors for cerebral aneurysms and their rupture are hypertension and tobacco use. Her hypertension is well controlled by the amlodipine. Smoking cessation is indicated to prevent further aneurysmal expansion and rupture.

Neither aneurysmal clipping nor endovascular coiling is necessary because the aneurysm is less than 12 mm and located in the anterior circulation, which suggests a low risk of rupture (0.05% annually). The surgical morbidity associated with either technique is too great given the low risk of rupture. Repeat neuroimaging on an annual basis can be considered to track any change in the aneurysm's size.

The calcium channel blocker nimodipine has been shown to improve outcomes in SAH and is the standard of care for all patients with aneurysmal SAH. SAH has been ruled out in this patient, whose blood pressure is well controlled by amlodipine. No evidence suggests that switching to nimodipine from amlodipine will prevent aneurysmal expansion or rupture.

Question 73

A 59-year-old man is evaluated for a 10-month history of hand tremor. The tremor is more prominent when he is tired, anxious, or walking. He also reports occasional difficulty with fine-motor movements, a deterioration of his handwriting, and a softening of his voice. His gait is not magnetic, and he has had no problem with balance or falls. The patient does not have urinary incontinence or dementia. His paternal grandfather had essential tremor and his paternal aunt had Parkinson disease.

On physical examination, vital signs are normal. Facial expression is normal, and his voice is low in volume but not tremulous. With the patient at rest, a low-frequency tremor is noted in the right hand and chin. With the arms in an outstretched position, a bilateral tremor emerges after a delay of several seconds that is more prominent on the right side. Finger-to-nose testing reveals a mild bilateral tremor that does not worsen near the target. Rapid alternating movements of the right upper and lower extremities become slower and shorter in amplitude with repetition. Muscle tone is increased bilaterally, with step-wise resistance to passive movements. Gait is normal, but arm swing is decreased and a tremor emerges on the right side during ambulation.

Which of the following is the most appropriate next step in confirming the diagnosis?

A

Dopamine transporter scan

B

MRI of the brain

C

Needle electrode electromyography

D

No further testing

Correct Answer: D

Educational Objective: Diagnose early Parkinson disease.

Key Point

The diagnosis of Parkinson disease can be made on the basis of clinical findings and requires the presence of bradykinesia and at least one of the other cardinal features of resting tremor, rigidity, or postural instability.

This patient most likely has early Parkinson disease (PD) on the basis of his clinical examination findings and does not require additional diagnostic testing. This diagnosis requires the presence of bradykinesia (in this patient, the decrements in speed and amplitude of repetitive movements) and at least one other cardinal feature (resting tremor, rigidity, or postural instability, with only postural instability absent in this patient). In addition, the absence of atypical features, such as early dementia, early falls, vertical gaze palsy, or prominent dysautonomia, is consistent with the diagnosis of PD. Reemergence of a resting tremor with posturing and ambulation also is seen in PD. The presence of bilateral kinetic tremor, although more typical of essential tremor, is still consistent with this diagnosis. Further diagnostic testing is not necessary in this patient before a diagnosis can be made.

A dopamine transporter scan can confirm degeneration of nigrostriatal dopaminergic terminals in Parkinson disease and differentiate between Parkinson disease and essential tremor in patients in whom the diagnosis cannot be made on clinical grounds (which is not the case in this patient). The sensitivity of this expensive test, however, is not superior to that of expert clinical assessment.

An MRI of the brain can be used to assess for vascular parkinsonism and hydrocephalus but should not be obtained before a clinical diagnosis is made. This patient does not have symptoms of vascular parkinsonism (predominant lower extremity involvement, gait impairment, and a step-wise course) or normal pressure hydrocephalus (the triad of gait impairment, urinary incontinence, and cognitive impairment), which makes these diagnoses unlikely.

Needle electrode electromyography can be helpful in studies of nerve and muscle disease but has no role in the diagnosis of Parkinson disease.

Question 74

A 52-year-old man is evaluated for worsening leg stiffness and pain. He has secondary progressive multiple sclerosis with associated chronic gait instability, leg weakness, spasticity, and urinary frequency. The patient reports an upper respiratory tract infection over the past week with nasal congestion and rhinorrhea and a mild, nonproductive cough. His leg stiffness and urinary frequency worsened shortly after the onset of respiratory symptoms but have persisted despite improvement in his congestion, rhinorrhea, and cough. Medications are interferon beta-1b, a vitamin D supplement, dalfampridine, tizanidine, and oxybutynin.

On physical examination, temperature is 37.8 °C (100.0 °F), blood pressure is 139/58 mm Hg, and pulse rate is 98/min. The nasal passages show moderate edema, and postnasal drip is present in the posterior oropharynx. The lungs are clear. Lower extremity spasticity and weakness are noted. All other physical examination findings are unremarkable.

Urinalysis is negative for leukocyte esterase and nitrite.

Bladder ultrasonography shows a postvoid residual urine volume of 180 mL.

Which of the following is the most appropriate treatment?

A

Amoxicillin-clavulanate

B

Increased dosage of oxybutynin

C

Methylprednisolone

D

Supportive care and clinical observation

Answer & Critique

Correct Answer: D

Educational Objective: Treat a pseudorelapse of multiple sclerosis, differentiating it from an actual relapse.

Key Point

A pseudorelapse of multiple sclerosis is a worsening of baseline neurologic symptoms or recurrence of previous symptoms that occurs in the setting of physiologic stressors, such as a superimposed infection.

This patient should be treated with supportive care and clinical observation. His clinical picture is consistent with a likely viral upper respiratory tract infection, which is causing a pseudorelapse of his multiple sclerosis (MS). MS pseudorelapses involve a worsening of baseline neurologic symptoms (or recurrence of previous symptoms) that occurs in the setting of physiologic stressors. In this patient, the viral syndrome and associated systemic inflammatory response are the underlying cause of the pseudorelapse. Supportive treatment of these symptoms and observation to ensure that the patient returns to baseline status is the most appropriate management to avoid unnecessary treatments or changes in medication. Because actual inflammatory relapses can sometimes be triggered by pseudorelapses (and similar causes), treatment with glucocorticoids can be considered if improvement does not occur within days of resolution of the causative condition.

The patient most likely has a viral upper respiratory tract infection, with no evidence of a urinary tract infection. Without evidence of bacterial infection, antibiotic therapy, such as administration of amoxicillin-clavulanate, is not indicated.

The increased postvoid residual urine volume suggests that this patient has moderate urinary retention. An increase in the oxybutynin dosage would cause relaxation of the muscles of the bladder wall and would likely worsen the patient's retention.

Although glucocorticoid therapy might be appropriate therapy for a true MS relapse, treatment with methylprednisolone in this patient with a likely pseudorelapse is inappropriate.

Question 75

A 57-year-old man is evaluated in the ICU 7 days after admission for a subarachnoid hemorrhage. An initial noncontrast head CT scan obtained in the emergency department showed a diffuse subarachnoid hemorrhage at the base of the brain that was thickest over the left hemisphere and accompanied by hydrocephalus. An external ventricular drain was placed to treat the hydrocephalus, and he subsequently underwent successful clipping of a 9-mm aneurysm of the left posterior communicating artery. Oral nimodipine was initiated.

On physical examination, temperature is 37.8 °C (100.1 °F), blood pressure is 138/78 mm Hg, pulse rate is 78/min, and respiration rate is 12/min. Neurologic examination shows an extremely somnolent patient who cannot follow commands and is unable to move the right arm and leg; on initial neurologic examination in the emergency department, the patient responded to loud noises, was able to follow simple commands, was oriented to time and place, and exhibited briskly reactive pupils and right arm drift.

Results of standard laboratory studies are normal.

Which of the following is the most appropriate next diagnostic test?

A

CT angiography of the brain

B

Electroencephalography

C

Lumbar puncture

D

MRI of the brain

Answer & Critique

Correct Answer: A

Educational Objective: Select the appropriate diagnostic test to evaluate for complications after subarachnoid hemorrhage.

Key Point

Cerebral vasospasm is a potential complication of subarachnoid hemorrhage that most often occurs 5 to 10 days after the hemorrhage and is best detected by CT angiography of the brain.

This patient should undergo CT angiography of the brain to assess for cerebral vasospasm. He is now at day 7 after a subarachnoid hemorrhage due to a left middle cerebral artery aneurysm. In the first 48 hours after a subarachnoid hemorrhage, rebleeding from an unsecured aneurysm and hydrocephalus are the principal causes of neurologic deterioration. This patient's aneurysm has been successfully clipped, and hydrocephalus is being managed with the use of an external ventricular drain. Potential neurologic complications after the first 48 hours include seizures, hydrocephalus, infection, and symptomatic cerebral vasospasm; the incidence of cerebral vasospasm peaks on days 5 to 10 after a hemorrhage. Cerebral vasospasm can manifest as a decline in neurologic function in patients who are awake enough for a neurologic examination. Although transcranial Doppler ultrasonography may reveal a vasospasm, CT angiography is more sensitive at detecting vasospasm that can be treated with the initiation of vasopressors to augment the blood pressure or with endovascular treatment in more refractory cases. CT angiography has the additional benefit of imaging the brain parenchyma for evidence of cerebral edema or infarction and the ventricles for evidence of hydrocephalus that may be amenable to shunting.

Electroencephalography (EEG) is inappropriate as the next diagnostic step in this patient with an aneurysmal subarachnoid hemorrhage. Convulsive and nonconvulsive status epilepticus is common and underdiagnosed after hemorrhagic stroke and is associated with poor neurologic outcome. If imaging does not identify a clear cause of the patient's decline that can be treated with medical or surgical therapy before irreversible damage occurs, then continuous EEG monitoring may help in diagnosing seizures.

Lumbar puncture may be useful for measuring intracranial pressure in this patient with an external ventricular drain. However, repeat imaging would first be required, independent of the presence of the drain, to rule out mass effect that could precipitate cerebral herniation after a lumbar puncture.

MRI requires too long a time to complete in the setting of a neurologic emergency and may not adequately detect arterial narrowing. Vasospasm is more readily detected with CT angiography.

Question 76

A 42-year-old man is evaluated for nighttime cramping and crawling sensations in his calves. He experiences these symptoms in the late evening, especially when watching television or getting ready for bed. At times, he feels an urge to stand up and pace around the room, which provides brief relief of symptoms. He has had no pain, weakness, or excessive daytime sleepiness. His mother has similar symptoms. His only medication is loratadine for seasonal allergies.

On physical examination, vital signs are normal. No abnormal movements are noted, and testing of deep tendon reflexes and sensation shows no anomalies.

Results of standard laboratory testing include a normal complete blood count and a serum ferritin level of 120 ng/mL (120 µg/L).

Which of the following is the most appropriate treatment?

A

Iron supplementation

B

Pentoxifylline

C

Ropinirole

DZolpidem

Answer & Critique

Correct Answer: C

Educational Objective: Treat restless legs syndrome.

Key Point

Dopamine agonists, such as ropinirole, pramipexole, or rotigotine, are first-line treatment for restless legs syndrome.

This patient has restless legs syndrome (RLS) and should be treated with ropinirole. Dopamine agonists, such as ropinirole, pramipexole, or rotigotine, are first-line treatments for RLS. This syndrome is characterized by the clinical features of abnormal sensations in the lower extremities, an urge to move the extremities in response to these sensations (with movement resulting in a transient relief of symptoms), emergence of symptoms at rest, and a circadian pattern (with symptoms more prominent at night). Diagnosis is clinical and based on history. Additional treatment options include gabapentin, gabapentin enacarbil, levodopa, and opioids.

Patients with RLS should be screened for iron deficiency. Iron supplementation can improve or resolve the symptoms of RLS in patients with iron deficiency and those with low-normal (15-45 ng/mL [15-45 µg/L]) serum ferritin levels. This patient's serum ferritin level is well above this range, and no evidence suggests that iron supplementation in this setting is beneficial.

Pentoxifylline is a peripheral vasodilator used in the treatment of peripheral arterial disease. Arterial insufficiency is not associated with RLS, and nothing suggests its presence in this patient. Therefore, this treatment is not indicated.

Zolpidem may help with insomnia but does not treat the underlying problem of RLS.

Question 77

A 71-year-old man is evaluated for progressive memory decline. In the past 3 years, he has noticed increasing word-finding difficulties and forgetfulness; he now requires frequent reminders to keep track of appointments. He has remained independent in activities of daily living, except for having to hire an accountant this year to file his taxes. His wife, who accompanied him to the appointment, reports that he is more irritable and impatient than before. The patient describes his mood as upbeat and says he has had no feelings of sadness or hopelessness. He has hyperlipidemia controlled with atorvastatin. His paternal uncle died of Alzheimer disease in his 80s.

On physical examination, vital signs are normal. The patient scores 27/30 on a Mini–Mental State Examination, losing points in the recall section. All other physical examination findings, including those from a neurologic examination, are normal.

Results of laboratory studies, including a complete blood count, a comprehensive metabolic profile, thyroid function tests, and measurement of serum vitamin B_{12} level, are normal.

Which of the following is the most appropriate next step in management?

A

Amyloid PET imaging

B

Brain MRI

C

Carotid Doppler ultrasonography

D

Determination of apolipoprotein E (*APOE ε4*) status

E

Fluorodeoxyglucose-PET imaging of the brain

Answer & Critique

Correct Answer: B

Educational Objective: Evaluate mild cognitive impairment.

Key Point

Structural neuroimaging studies, specifically head CT and brain MRI, can play a key role in the routine diagnostic evaluation of patients with established cognitive impairment to exclude structural lesions of the brain, such as strokes, hematomas, brain tumors, or other mass lesions.

This patient should have an MRI of the brain. He most likely has mild cognitive impairment (MCI), as evidenced by cognitive difficulties that are greater than those typical of normal aging but do not impair activities of daily living and have minimal effect on instrumental activities of daily living. MCI is a clinical diagnosis made exclusively on the basis of history and the results of cognitive testing. Although neuroimaging cannot be used to detect whether or not a cognitive disorder is present, structural neuroimaging studies, specifically head CT and brain MRI, can play a key role in the routine diagnostic evaluation of patients with established cognitive impairment to exclude structural lesions of the brain, such as strokes, hematomas, brain tumors, or other mass lesions.

Amyloid PET imaging allows for in vivo detection of amyloid plaques, which are a core pathologic feature of Alzheimer disease. However, positive results are not synonymous with the presence of Alzheimer disease because cognitively normal persons can have abnormal scans. Amyloid PET imaging may provide prognostic information in patients with MCI by identifying those whose cognitive impairment may be related to underlying Alzheimer disease pathology, but much more research is still required before the routine use of this technology in clinical practice.

Screening for carotid stenosis with ultrasonography or any imaging modality has no role in the routine evaluation of cognitive impairment in an asymptomatic patient. An asymptomatic patient in this context is one without previous hemispheric neurologic symptoms—such as transient ischemic attack, stroke, or amaurosis fugax—or the presence of a carotid bruit on examination.

The apolipoprotein E gene (*APOE ?4*) located on chromosome 19 has been identified as a genetic risk factor for late-onset Alzheimer disease. *APOE ?4* genotyping has marginal additive value over

clinical diagnoses but is neither necessary nor sufficient to predict who will develop Alzheimer disease and thus is not recommended for broad clinical use.

A fluorodeoxyglucose-PET scan of the brain or any other metabolic scan of the brain cannot determine if a patient's cognitive symptoms indicate cognitive impairment. Abnormal results of fluorodeoxyglucose-PET scanning also occur in persons who are cognitively normal. Although these abnormal results may indicate a future risk of cognitive impairment, this relationship has not been established.

Question 78

A 75-year-old woman is evaluated in the emergency department 90 minutes after onset of right arm weakness and an inability to speak. The patient has atrial fibrillation, hypertension, and dyslipidemia. Medications are warfarin, nifedipine, hydrochlorothiazide, and simvastatin.

On physical examination, blood pressure is 148/78 mm Hg and pulse rate is 86/min and irregular. On neurologic examination, global aphasia, right arm paralysis, antigravity movement in the right leg, left gaze preference, and decreased blink response to threat from the right side are noted. Her score on the National Institutes of Health Stroke Scale is high at 22, indicating a severe stroke.

Results of standard laboratory studies include an INR of 1.4 but are otherwise normal.

A noncontrast CT scan of the head shows hyperdensity in the territory of the left middle cerebral artery but is otherwise normal.

After exclusion criteria are ruled out, treatment with intravenous recombinant tissue plasminogen activator (rtPA) is begun 40 minutes after arrival at the emergency department; 60 minutes into the infusion, blood pressure is 168/78 mm Hg, pulse rate is 84/min and irregular, and repeat neurologic examination shows paralysis of the right leg.

Which of the following is the most appropriate next step in management?

A

Intra-arterial thrombectomy

B

Intravenous labetalol

C

Rectal aspirin

D

Repeat noncontrast CT of the head

Answer & Critique

Correct Answer: D

Educational Objective: Diagnose an acute complication of thrombolytic therapy.

Key Point

Hemorrhage after thrombolysis for ischemic stroke can be detected on a noncontrast CT scan of the head.

This patient should undergo repeat noncontrast CT of the head. She had an ischemic stroke that was likely due to subtherapeutic anticoagulation. Findings from physical examination, notably an elevated National Institutes of Health Stroke Scale (NIHSS) score, and the initial CT scan of the head suggest a large cerebral infarction in the entire territory of the left middle cerebral artery. She was appropriately given intravenous recombinant tissue plasminogen activator within the recommended treatment window because of the high risk of a poor neurologic outcome. At the time of treatment, she did not meet any exclusion criterion for thrombolysis, such as an elevated blood pressure or an INR greater than 1.7. The patient has several risk factors for intracerebral hemorrhage after thrombolysis, including a high NIHSS score and a cardioembolic cause of the stroke. Any change in the neurologic examination, particularly in patients treated with thrombolysis, should prompt consideration of hemorrhage, which is associated with a high mortality rate. Hemorrhage after thrombolysis can be detected on a noncontrast CT scan of the head.

Intra-arterial thrombectomy is inappropriate in this patient. The new right-leg paralysis noted in the second neurologic examination is most concerning for intracerebral hemorrhage after thrombolysis. However, the benefit of intra-arterial treatment modalities, after or instead of intravenous thrombolysis, has not been established in randomized clinical trials.

This patient also should not be given intravenous labetalol. Administering treatment to lower her blood pressure is inappropriate because her blood pressure is already less than the recommended target of 180/105 mm Hg after thrombolysis.

Aspirin is appropriate stroke therapy in patients not eligible for thrombolysis and can be administered rectally in patients who are unable to swallow. However, in patients who have received thrombolysis, early administration of antiplatelet agents can increase the risk of hemorrhage. In addition, although aspirin is associated with a reduction in recurrent stroke risk when administered within 48 hours of ischemic stroke onset, aspirin has not been shown to prevent or reverse neurologic worsening.

Question 79

A 30-year-old woman is evaluated for difficult-to-treat migraine. She has had severe headaches, usually on the first day of menses, since menarche. The pain is hemicranial, pulsatile, and associated with severe nausea and vomiting but no aura. She frequently awakens with the attack already in progress. Ibuprofen was helpful in controlling migraine pain during her teenage years and early 20s but was replaced 5 years ago by oral eletriptan after the pain was no longer controlled; this drug now also is ineffective in relieving symptoms. A trial of oral frovatriptan for menstrual migraine relief also has been unsuccessful. The patient reports receiving intravenous dihydroergotamine and magnesium at an urgent care facility twice in the past 3 months as treatment of refractory headaches.

On physical examination, blood pressure is 98/60 mm Hg and pulse rate is 72/min. All other physical examination findings, including those from a neurologic examination, are normal.

Which of the following is the most appropriate next step in treatment?

A

Butalbital

B

Hydrocodone

C

Naproxen

D

Orally dissolvable rizatriptan

E

Subcutaneous sumatriptan

Choose an

Answer & Critique

Correct Answer: E

Educational Objective: Treat acute refractory migraine.

Key Point

Self-administered subcutaneous sumatriptan is appropriate as therapy for migraine without aura in patients not responding to NSAIDs or oral triptans, especially those with vomiting.

The patient should be treated with subcutaneous sumatriptan for migraine without aura. She no longer responds to NSAIDs and oral triptans. The headaches are associated with emesis, and she is awakening with attacks. Migraine episodes have been so severe that she has visited an urgent care facility recently for parenteral treatment of refractory migraine. Self-administered injectable migraine medications would be of value for this patient. Although nasal spray options exist for several acute medications, they are less potent than their injectable counterparts. According to guidelines, no first-line agent for acute migraine treatment is available in suppository form.

Neither butalbital compounds nor opioids (such as hydrocodone) are recommended as first-line treatments of recurrent headache disorders. Little evidence of benefit in acute migraine exists for either class of drugs, and both contribute to an increased future risk of transformation into chronic migraine, compared with first-line agents.

Evidence supports the use of naproxen in the management of acute migraine, and the drug is listed by evidence-based guidelines as first-line therapy. In the setting of migraine that occurs upon awakening or with vomiting, however, it is unlikely to be beneficial, especially in a patient who has not responded to another NSAID or oral triptan.

The orally dissolvable versions of rizatriptan and zolmitriptan require gastrointestinal absorption and thus should not be used in the setting of migraine with vomiting.

Question 80

A 44-year-old man is evaluated in the emergency department for a severe global headache and blurred vision. Two hours ago, he was struck with a pipe in the right frontotemporal region and anterior neck and knocked to the ground but did not lose consciousness. While describing the assault, the patient becomes stuporous.

On physical examination, blood pressure is 150/100 mm Hg, pulse rate is 50/min, and respiration rate is 10/min. Continued stupor is noted, as are right pupillary dilation, palsy of the oculomotor nerve (cranial nerve III), and an extensor plantar response on the left. The patient withdraws from pain more weakly on the left than the right. No other cranial nerve abnormalities are detected.

Which of the following is the most likely diagnosis?

A

Epidural hematoma

B

Left internal carotid artery dissection

C

Postconcussion syndrome

D

Posttraumatic seizure

Answer & Critique

Correct Answer: A

Educational Objective: Diagnose a posttraumatic epidural hematoma.

Key Point

Traumatic epidural hematoma classically presents with precipitous neurologic decline after head trauma; common symptoms are severe headache and vomiting, with possible impairment of consciousness developing immediately or after a lucid interval.

This patient most likely has an epidural hematoma. Traumatic epidural hematoma classically presents with precipitous neurologic decline after head trauma. Most patients with this diagnosis have a skull fracture with associated rupture of an underlying artery, typically the middle meningeal artery. Blood under arterial pressure accumulates between the inner table of the skull and the dural membranes. The most common symptoms are severe headache and vomiting. Impairment of consciousness may develop immediately or after a lucid interval. Uncal or subfalcine brain herniation can occur and is characterized by ipsilateral occulomotor nerve (cranial nerve III) palsy, contralateral paresis, and stupor or coma. Hypertension with bradycardia (the Cushing response) can be another sign of increased intracranial pressure. A CT scan of the head confirms the diagnosis, and immediate surgical evacuation is required. Mortality rates are commonly reported to be 10% to 20%.

Dissection of the left internal carotid artery typically results in ipsilateral Horner syndrome with ptosis, miosis, and anhidrosis but not oculomotor nerve (cranial nerve III) palsy. Contralateral hemiparesis could result if a secondary stroke were to occur in the left frontal lobe after the dissection, but rapidly declining consciousness would be unexpected.

Postconcussion syndrome is defined by a constellation of neurologic, psychological, and constitutional symptoms without significant abnormalities on physical examination. Minor neurologic findings noted on the examination of a patient with mild traumatic brain injury may include ocular convergence insufficiency or mild ataxia, but typically examination findings are normal. This patient's clinical findings do not fit this pattern.

Seizures occur in approximately 5% of persons hospitalized for acute head trauma. They may be classified as “immediate” if occurring within the first 24 hours, “early” if noted within the first week, or “late” if occurring more than 1 week after the injury. Half of the seizures occurring within the first week will occur in the first 24 hours, and the risk decreases with time. Some correlation between the severity of injury and the risk of posttraumatic seizures exists. This patient shows no signs of involuntary motor activity, so convulsive status epilepticus is not present. Nonconvulsive status epilepticus might manifest as stupor, but the presence of focal cranial nerve and motor deficits in this patient is more indicative of a progressive structural lesion.

Question 81

A 22-year-old woman is evaluated for a 2-year-history of abnormal involuntary movements. She describes these movements as a quick elevation of the left shoulder followed by a rolling movement of the neck from side to side. The patient is able to suppress the movements completely for brief periods but then feels pressure building at the left shoulder and the urge to release it. She has experienced no other abnormal movements recently but reports uncontrollable blinking 5 years ago and occasional facial grimacing 3 years ago, both of which resolved after 2 years. She also recently has exhibited obsessive-compulsive behavior, such as repeatedly checking that the oven is turned off and all the doors are locked. The patient has anxiety disorder treated with cognitive behavioral therapy. Her father and brother have facial twitching. She takes no medication.

On physical examination, vital signs are normal. The patient is asked to relax and not suppress any movement, after which the left shoulder quickly elevates, followed by the described repeated slower rolling movement of the neck. In the interval between movements, the neck is at midline with no evidence of pulling, tilting, or turning. The movements are more frequent initially but completely disappear during the second half of the visit. She often clears her throat, even during conversation, and frequently blinks. Neurologic examination findings are otherwise unremarkable.

Which of the following is the most likely diagnosis?

A

Chorea

B

Dystonia

C

Myoclonus

D

Tic disorder

Answer & Critique

Correct Answer: D

Educational Objective: Diagnose a tic disorder.

Key Point

Tics are repetitive, stereotyped, suppressible movements typically preceded by an abnormal sensation (premonitory urge).

This patient's clinical presentation is most consistent with a tic disorder. Tics are repetitive, stereotyped, suppressible movements typically preceded by an abnormal sensation (premonitory urge). She previously has experienced simple motor tics and has a positive family history of facial twitching. The presence of vocal (repetitive throat clearance) and complex motor (shoulder elevation followed by neck rolling) tics, the persistence of symptoms for 1 year, and the comorbid obsessive-compulsive disorder are all consistent with Tourette syndrome. Tics can wax and wane, and old tics can be replaced by new ones over time, but at any given time, a limited number of stereotyped movements are present during clinical examination.

Chorea involves typically random, diffuse, and nonsuppressible involuntary abnormal movements. The focal distribution, suppressibility, and stereotyped character of this patient's movements make chorea unlikely.

Dystonia consists of patterned and directional movements limited to certain parts of the body. However, dystonia is typically sustained and nonsuppressible. The presence of vocal tic, the premonitory urge, and the long history of waxing and waning of various types of movements in this patient also make dystonia unlikely.

Myoclonus consists of a single, rapid, shocklike muscle jerk. Complex stereotyped movements (such as shoulder elevation followed by neck rolling) and suppressibility are inconsistent with myoclonus.

Question 82

A 55-year-old man is evaluated in the hospital for an episode of painful tingling in the right arm followed by clonic jerking of that arm lasting 3 minutes. Medical history is significant for non–small cell lung cancer diagnosed 1 year ago and treated with surgical resection. He was evaluated in the emergency department 1 week ago for a new-onset headache, at which time an isolated brain metastasis in the left parietal area was identified. He subsequently was admitted for planned surgical resection of this lesion, adjuvant local radiation, and systemic chemotherapy.

On physical examination, temperature is 36.6 °C (97.9 °F), blood pressure is 120/92 mm Hg, pulse rate is 105/min, and respiration rate is 16/min. Right inferior quadrantanopia, right neglect, increased tone in the right arm and leg, and a plantar extensor response in the right toe are noted.

An MRI of the brain shows a stable contrast-enhancing lesion in the left parietal lobe consistent with the patient's known metastasis.

An electroencephalogram shows left hemispheric slowing with no evidence of epileptiform discharges.

Which of the following is the most appropriate management?

A

Carbamazepine

B

Phenytoin

C

Valproic acid

D

Deferral of antiepileptic drug therapy

Answer & Critique

Correct Answer: C

Educational Objective: Treat seizures in a patient with a brain tumor.

Key Point

In patients with metastatic brain tumors and one or more seizures, antiepileptic drug regimens that do not induce hepatic enzymes and thus have limited interaction with commonly used chemotherapy regimens are favored.

This patient should be treated with valproic acid. In patients with brain tumors and one or more seizures, antiepileptic drug (AED) regimens that do not induce hepatic enzymes and thus have limited interaction with commonly used chemotherapy regimens are favored. Valproic acid is a non–enzyme-inducing AED that is appropriate to treat this patient. Other AEDs that would be reasonable to use include lacosamide, lamotrigine, and levetiracetam.

Carbamazepine and phenytoin are enzyme-inducing AEDs that can diminish the efficacy of the chemotherapy and other drugs this patient may receive. Additionally, because they are metabolized by the same enzyme pathways, chemotherapeutic agents also may alter AED levels unpredictably, which makes them potentially less effective in controlling seizures.

Deferring AED therapy in this patient is not appropriate. He had a clear focal seizure, and the presence of a known brain lesion puts him at risk for subsequent seizures. However, AED treatment is not appropriate as prophylaxis in patients with brain tumors who have not had any clinical seizures.

Question 83

A 66-year-old man is evaluated in the emergency department for increasingly difficult-to-manage behaviors. According to his son with whom he lives, he has exhibited intermittent forgetfulness, gotten lost while driving on familiar routes, and had brief but frequent periods of nonsensical speech, excessive daytime sleepiness, and an inability to use familiar objects during the past year. Over the past 3 months, the patient has had increasing visual hallucinations and paranoia accompanied by agitation and restlessness. Medical history is significant for mild depression. His only medication is sertraline. A depression screen is negative for a depressed mood.

On physical examination, temperature is 36.8 °C (98.2 °F), blood pressure is 135/70 mm Hg, pulse rate is 80/min, respiration rate is 16/min, and oxygen saturation is 98% on ambient air. General physical examination findings are normal. Neurologic examination shows an agitated man with masked facies, a soft voice, postural instability, and a slow gait. He scores 24/30 on the Mini-Mental State Examination, missing points on orientation to time and place, delayed recall, and figure drawing.

The patient is given haloperidol in the emergency department to treat the agitation, which results in worsening agitation and limb and neck stiffness.

Which of the following is the most likely diagnosis?

A

Alzheimer disease

B

Delirium

C

Dementia with Lewy bodies

D

Major depression with psychotic features

Answer & Critique

Correct Answer: C

Educational Objective: Diagnose dementia with Lewy bodies.

Key Point

Core features of dementia with Lewy bodies are fluctuating attention and alertness; recurrent, well-formed visual hallucinations; or spontaneous parkinsonism.

This patient most likely has dementia with Lewy bodies, the second most common cause of degenerative dementia. Core features of dementia with Lewy bodies are fluctuating attention and alertness; recurrent, well-formed visual hallucinations; and spontaneous parkinsonism. Sensitivity to neuroleptic medications also is commonly seen. Suggestive features include rapid eye movement sleep behavior disorder and low dopamine transporter uptake in the basal ganglia on single-photon emission CT or PET scans. The patient's features of cognitive fluctuations (episodic disorganized speech and functional disability, daytime sleepiness), parkinsonism, visual hallucinations, and severe sensitivity to haloperidol all support a diagnosis of dementia with Lewy bodies.

Although visual hallucinations and parkinsonism can occur in Alzheimer disease, these features generally present relatively late in the disease course. Severe sensitivity to neuroleptic medications also is less common in Alzheimer disease than dementia with Lewy bodies. Alzheimer disease is predominantly characterized by a decline in memory that can be accompanied by deficits in other cognitive domains. Typical behavioral changes in the earlier stages of Alzheimer disease include irritability, anxiety, and depression.

Delirium is characterized by disturbances of attention, cognition, and perception, with fluctuations in symptoms during the day. These disturbances typically develop over the course of hours to days, rather than over 1 year as occurred in this patient. A careful history obtained from a reliable informant often easily distinguishes delirium from dementia with Lewy bodies.

Major depression with psychotic features is characterized by hallucinations, more often auditory than visual, and delusions that are typically mood congruent, such as guilt, nihilism, or deserved punishment. Although the patient is being treated for depression, no evidence that supports a

diagnosis of major depression, such as suicidal ideation, hopelessness, or guilt, has been reported.

Question 84

A 36-year-old woman is evaluated for a 1-week history of recurrent episodes of facial pain that are 1 to 3 seconds in duration and occur spontaneously dozens of times throughout the day. The pain is sharp, severe, and located in the right infraorbital area. During this same period, she has developed worsening bilateral lower extremity weakness and urinary incontinence. The patient has an 18-year history of relapsing-remitting multiple sclerosis treated with interferon beta-1a; she also takes baclofen to control spasticity. She has had no nausea, photophobia, phonophobia, nasal congestion, nasal drainage, or ocular/visual changes.

On physical examination, blood pressure is 100/64 mm Hg and pulse rate is 80/min. Moderate bilateral lower extremity weakness and hyperreflexia are noted. Sensory spinal cord level for pain and temperature is T6. Plantar responses are extensor bilaterally. Internuclear ophthalmoplegia is noted, but other findings from an examination of the cranial nerves are unremarkable.

Results of laboratory studies, including a comprehensive metabolic profile, a complete blood count, and urinalysis, are normal.

Which of the following is the most likely cause of the facial pain?

A

Chronic paroxysmal hemicrania

B

Herpes zoster

C

Primary stabbing headache

D Trigeminal neuralgia

Answer & Critique

Correct Answer: D

Educational Objective: Diagnose trigeminal neuralgia.

Key Point

Trigeminal neuralgia typically results in brief episodes of lancinating pain affecting either the second or third distribution of the trigeminal nerve (cranial nerve V_2 or V_3); the pain can occur spontaneously or be triggered by sensory stimulation of the face or mouth.

This patient has developed trigeminal neuralgia. Although more common among older patients, trigeminal neuralgia can be seen in young adults, particularly those with multiple sclerosis. Affected patients describe brief episodes of lancinating pain affecting either the second or third distribution of the trigeminal nerve (cranial nerve V_2 or V_3). The pain may occur spontaneously or be triggered by sensory stimulation of the face or mouth. The diagnosis is made clinically. Brain MRI may be indicated in patients with atypical presentations, including those developing symptoms in young adulthood. As many as 15% of patients with trigeminal neuralgia may have a structural explanation for their disease, such as cerebellopontine angle tumors in older patients or demyelinating disease in younger patients. Brain MRI is also indicated in the course of surgical evaluation, if appropriate. Glucocorticoids are typically ineffective. Carbamazepine is the drug of choice for initial management, with a greater than 50% response rate. Oxcarbazepine, a structural derivative of carbamazepine, is also effective and has fewer adverse effects and drug interactions but is a more expensive medication.

Chronic paroxysmal hemicrania is typically expressed along the first branch of the trigeminal nerve (cranial nerve V_1). Pain attacks are brief but generally last a mean of 15 minutes rather than seconds and may recur between 8 to 40 times daily. The diagnosis also requires concomitant ipsilateral autonomic findings, such as tearing, nasal congestion, or rhinorrhea, none of which this patient has.

The eruption of herpes zoster is preceded by a prodrome of constant pain or burning, commonly for up to several days. The patient's intermittent sharp facial pain is most consistent with trigeminal neuralgia.

Primary stabbing headaches are brief paroxysms of pain lasting seconds, without associated autonomic features. The face is typically spared. This patient's pain does not fit this description.

Question 85

A 64-year-old woman is evaluated for persistent myopathy. Polymyositis was confirmed by muscle biopsy 6 months ago. High-dose prednisone was started, with almost full recovery within 4 months; the glucocorticoid was subsequently tapered to daily low-dose prednisone. For the past month, she has experienced a recurrence of weakness in the deltoid and hip flexor muscle groups. Her only medication is prednisone, 20 mg.

On physical examination, blood pressure is 132/80 mm Hg and pulse rate is 80/min; BMI is 35. Neck extensor, arm abductor, elbow extensor, hip flexor, and knee extensor muscles are moderately weak; distal muscle strength is normal. Muscle tone is flaccid, but sensory examination findings are normal. Deep tendon reflexes are absent at the triceps muscle and patella but normal elsewhere. The plantar response is flexor. Assessment of cranial nerves and mental status shows no abnormalities.

Results of laboratory studies show a serum creatine kinase level of 80 U/L.

Which of the following is the most appropriate management?

A

Add intravenous immune globulin

B

Increase prednisone dosage

C

Taper prednisone dosage

D

Repeat muscle biopsy

Answer & Critique

Correct Answer: C

Educational Objective: Adjust medication dosage in glucocorticoid-induced myopathy.

Key Point

Glucocorticoid tapering is the most appropriate method to distinguish between a flare of inflammatory myopathy and glucocorticoid-induced toxic myopathy in a patient with persistent myopathy.

Tapering the prednisone dosage while monitoring the patient's response is the most appropriate method to distinguish between weakness caused by a flare of inflammatory myopathy and glucocorticoid-induced toxic myopathy. The latter diagnosis is more likely in this patient with a normal serum creatine kinase level. In contrast, a flare of inflammatory myopathy, which can present the same way clinically, is associated with a marked increase in the serum creatine kinase level and evidence of irritable myopathy on electromyography (such as abnormal spontaneous necrosis or active muscle membrane damage from inflammation). If weakness improves after prednisone tapering, the patient should be given a glucocorticoid-free holiday or, if needed, switched to another agent. In contrast, if weakness worsens with tapering, an inflammatory flare should be suspected, and increasing the glucocorticoid dosage or adding another immunosuppressive therapy should be considered.

Intravenous immunoglobulin (IVIG) is a second-line therapy for severe inflammatory myopathies that are refractory to treatment with a glucocorticoid and at least one other immunosuppressive agent. Because glucocorticoid-induced myopathy is suspected in this patient, IVIG treatment is not warranted.

Increasing the prednisone dosage without evidence of active inflammation would be inappropriate and could worsen the patient's weakness, which is likely associated with glucocorticoid therapy.

A repeat muscle biopsy might show type 2 muscle fiber atrophy due to glucocorticoid myopathy, but these changes also are seen in disuse atrophy and other conditions and thus are nonspecific.

Biopsy is also likely to show inflammatory changes but is unlikely to provide a definitive differentiation between a flare of inflammatory myopathy and glucocorticoid-induced myopathy.

Question 86

A 49-year-old woman is evaluated in the emergency department 45 minutes after onset of right-sided weakness and loss of vision. She has dyslipidemia and hypertension. Medications are simvastatin and hydrochlorothiazide.

On physical examination, blood pressure is 160/88 mm Hg, pulse rate is 78/min and irregular, and respiration rate is 12/min. No carotid bruits are heard on cardiac examination. On neurologic examination, speech is fluent with occasional word-finding difficulties. A right inferior visual field deficit, right facial weakness, mild dysarthria, right arm pronator drift, and loss of pinprick sensation on the right arm and face are noted. No right leg weakness is detected. The National Institutes of Health Stroke Scale score is 7 (moderate stroke).

An electrocardiogram shows atrial fibrillation with no ST-segment or T-wave changes. A noncontrast CT scan of the head is normal.

The patient receives intravenous recombinant tissue plasminogen activator 50 minutes after arrival in the emergency department. Three hours after the infusion is completed, her blood pressure is 188/110 mm Hg and pulse rate is 68/min. Other physical examination findings are unchanged.

Which of the following is the most appropriate treatment?

A

Intravenous nicardipine

B

Oral aspirin

C

Subcutaneous heparin

D Sublingual nitroglycerin

Answer & Critique

Correct Answer: A

Educational Objective: Treat elevated blood pressure after recombinant tissue plasminogen activator therapy for stroke.

Key Point

After patients with acute ischemic stroke are treated with intravenous recombinant tissue plasminogen activator, their blood pressure should be maintained at less than 180/105 mm Hg to avoid intracerebral hemorrhage.

The patient should receive intravenous nicardipine in an attempt to lower her blood pressure to the target range. She met no exclusion criteria and was correctly treated with intravenous recombinant tissue plasminogen activator (rtPA) for an acute ischemic stroke within the optimal 3-hour window from onset of symptoms. Her blood pressure before treatment was less than 185/110 mm Hg, as recommended by guidelines. The most serious complication of thrombolysis with intravenous rtPA is intracerebral hemorrhage, which occurs in as many as 6% of patients. The main risk factors for hemorrhage after thrombolysis are a large-volume cerebral infarction, a high National Institutes of Health Stroke Scale score, a cardioembolic origin of the stroke, and protocol violations. The postthrombolysis protocol includes avoiding antiplatelet and anticoagulant agents for 24 hours until a repeat head CT scan shows no hemorrhage, frequent neurologic and vital sign evaluation, and maintenance of the blood pressure at less than 180/105 mm Hg. When the blood pressure exceeds this limit, as in this patient, intravenous labetalol or nicardipine is the best option to reduce the blood pressure and thereby avoid intracerebral hemorrhage.

Oral aspirin and subcutaneous heparin are inappropriate treatments for this patient at this point because antithrombotic medications should not be administered until follow-up CT of the head is obtained 24 hours after rtPA infusion is completed. If the repeat CT scan shows no hemorrhage, and no systemic bleeding complications have occurred, then aspirin should be initiated for secondary stroke prevention and deep venous thrombosis prophylaxis should be started with low-molecular-weight or unfractionated subcutaneous heparin.

Although sublingual nitroglycerin can lower blood pressure, the inability to rapidly titrate the dose to maintain a blood pressure of less than 180/105 mm Hg makes nonintravenous medications a

poor choice. Nitrates also have a relative contraindication in the treatment of blood pressure in acute stroke, particularly hemorrhagic stroke, because of the possibility of raising intracranial pressure.

Question 87

A 39-year-old woman is evaluated for worsening headaches. Headache episodes initially developed while she was in high school but have become increasingly severe and frequent over the past 3 years. She describes these recent headaches as an intense, hemicranial, throbbing pain that occurs two or three times per week and is associated with nausea and photophobia. For the past year, she has experienced additional daily episodes of dull, mild, global head pressure without associated features. The patient also has asthma and mild depression. She stopped taking over-the-counter analgesics 6 months ago when they became ineffective; other medications are albuterol and fluticasone.

On physical examination, blood pressure is 122/78 and pulse rate is 74/min; BMI is 22. Other physical examination findings, including those from a neurologic examination, are unremarkable.

An MRI of the brain is normal.

Which of the following is the most appropriate treatment?

A

Carbamazepine

B

Duloxetine

C

Propranolol

D

Topiramate

E

Verapamil

Answer & Critique

Correct Answer: D

Educational Objective: Treat chronic migraine.

Key Point

Topiramate and onabotulinumtoxinA are the only agents that have shown efficacy in studies of chronic migraine.

The patient should be treated with topiramate for chronic migraine, which is headache occurring on 15 or more days per month for more than 3 months. Chronic migraine is characterized by increasingly frequent attacks of migraine that are eventually accompanied by an interval milder headache. By definition, on at least 8 days of the month, the headache of chronic migraine must be severe, possess migraine features, or respond to migraine-specific therapy. The interval headache may have no migraine features and appear to be a tension-type or sinus headache. A medication overuse element is often present and may interfere with the efficacy of preventive and acute migraine treatments. Headache frequency and acute medication use of greater than 10 days per month are significant risk factors for transformation to chronic migraine. Because the development of secondary brain pathology also occasionally may contribute to the transformation to chronic migraine, MRI of the brain is indicated.

Topiramate has level A evidence of effectiveness in treating episodic migraine. Topiramate and onabotulinumtoxinA are the only agents that have shown efficacy in studies of chronic migraine. Topiramate is less expensive than onabotulinumtoxinA.

Carbamazepine is the drug of choice for treating trigeminal neuralgia but has shown no effect on migraine prevention.

Although the serotonin-norepinephrine reuptake inhibitor venlafaxine has demonstrated benefit in migraine prevention studies, no such data are available for duloxetine, which is in the same drug class and is used to treat major depressive disorder and generalized anxiety disorder.

Propranolol has level A evidence of effectiveness in the prevention of episodic migraine but has the potential to worsen both depression and asthma. No evidence supports it use for chronic migraine.

Verapamil is the treatment of choice in cluster headache prevention. The drug, however, has neither level A (effective) nor level B (probably effective) evidence supporting its use in migraine prevention.

Bibliography

Question 88

A 51-year-old woman is evaluated in the emergency department (ED) for increasingly agitated and paranoid behavior. Over the past 4 weeks, she has exhibited short-term memory loss and has been less organized and more confused, which necessitated her taking a leave from work. Her son also has noticed her occasionally sitting motionless, staring at nothing and smacking her lips. She was brought to the ED after she stopped eating because of a belief that someone was trying to poison her. The patient has no other personal medical history and no family history of dementia or psychiatric disorders. She takes no medication.

On physical examination, temperature is 36.1 °C (97.0 °F), blood pressure is 100/70 mm Hg, pulse rate is 70/min, and respiration rate is 16/min. The patient is agitated, with wandering attention. She does not know the date, often missing it by a decade. She can repeat three of three words but 5 minutes later does not recall any of them. Findings of cranial nerve examination are normal, as are muscle strength, coordination, and reflexes.

Serum sodium level is 128 mEq/L (128 mmol/L). All other results of laboratory studies, including a comprehensive metabolic profile and complete blood count, are normal.

An MRI shows increased flair signal in both mesial temporal regions. Continuous EEG monitoring reveals frequent temporal lobe seizures (8/day) occurring from both the left and right temporal lobes.

Which of the following is the most likely diagnosis?

A

Alzheimer disease

B

Human herpesvirus 1 encephalitis

C

Lewy body dementia

D

Paraneoplastic limbic encephalitis

Answer & Critique

Correct Answer: D

Educational Objective: Diagnose paraneoplastic limbic encephalitis.

Key Point

The subacute progression of the symptoms of personality change, psychosis, and seizures is most consistent with an antibody-mediated cause, such as a paraneoplastic antibody syndrome.

This patient has limbic encephalitis, or inflammation of the emotional and memory structures of the brain. The subacute progression of this patient's symptoms of personality change, psychosis, and seizures is most consistent with a paraneoplastic antibody syndrome, which is usually mediated by autoantibodies. Paraneoplastic limbic encephalitis is most commonly associated with lung tumors (usually small cell lung cancer), breast cancer, thymoma, germ cell tumors, and Hodgkin lymphoma. Patients frequently have the neurologic symptoms before discovery of the causative tumor. In this patient, the possible presence of the concomitant syndrome of inappropriate antidiuretic hormone secretion (SIADH), as suggested by the low serum sodium level, makes the particular diagnosis of anti-LG1 (formerly anti–voltage-gated potassium channel) antibody syndrome most likely because it is associated with both limbic encephalitis and SIADH. A definitive diagnosis is usually made after laboratory testing of serum and/or cerebrospinal fluid (CSF) for paraneoplastic antibodies in the appropriate clinical context. Treatment involves immunotherapy and treatment of the underlying tumor, if available. Although these syndromes traditionally have been characterized as “paraneoplastic” because they often are associated with an underlying cancer, many, including most anti-LG1 syndromes, are primarily autoimmune.

Although paranoia and seizures can be seen in Alzheimer disease, they typically occur late in the disease course. Alzheimer disease also is not generally associated with mesial temporal MRI changes.

Reactivation of human herpesvirus 1 also can cause an encephalitis with cognitive problems, psychiatric disturbance, and bitemporal seizures. However, the progression of this type of encephalitis is acute, occurring over days, not weeks. If not treated emergently, herpes encephalitis is lethal. Patients suspected of having human herpesvirus 6 encephalitis will need a

lumbar puncture to rule out other viral causes of limbic encephalitis, such as human herpesvirus 3 (varicella-zoster virus), human herpesvirus 8, and cytomegalovirus.

The course of Lewy body dementia is typically longer than that described in this patient. Also, the seizures and imaging findings would be atypical.

Question 89

A 90-year-old man is evaluated in the hospital for disorientation. He was admitted 5 days ago after having a myocardial infarction. Before hospitalization, he was living alone and functioning independently. Since hospitalization, the patient has had periods of daytime sleepiness alternating with periods of agitation. Medications are aspirin, clopidogrel, metoprolol, lisinopril, and atorvastatin.

On physical examination, temperature is normal, blood pressure is 130/82 mm Hg, pulse rate is 70/min, and respiration rate is 16/min. Cardiac examination shows an early systolic murmur and normal heart sounds. Neurologic evaluation shows sudden involuntary jerks of the upper extremities that increase in frequency when the arms are outstretched and wrists are extended. The patient is oriented to self and location but not to date and believes he has been hospitalized for only 1 day. He cannot spell the word “world” backwards, and his responses to questions are at times inappropriate or tangential. He requires frequent redirection during the interview and appears to be distracted by something on the wall. Findings from the rest of the physical examination are otherwise unremarkabl

Laboratory studies:	
Complete blood count	Normal
Liver chemistry studies	Normal
Glucose, fasting	Normal
Creatine kinase	Normal
Creatinine	2.9 mg/dL (256 µmol/L) (2.0 mg/dL [177 µmol/L] on admission)

Bottom of Form

Which of the following is the most likely diagnosis?

A

Delirium

B

Dementia

C

Nonconvulsive status epilepticus

D

Stroke

Answer & Critique

Correct Answer: A

Educational Objective: Diagnose delirium.

Key Point

Acute onset of cognitive dysfunction over hours to days, impairment of attention, disorganized thinking, and fluctuating mental status are core features of delirium, an underrecognized disorder in older patients who are hospitalized.

This patient most likely has delirium. Tests such as spelling a word backwards or reciting the days of the week in reverse are rapid ways to measure attention at the bedside. Frequent redirection during the course of an interview is another indicator of inattention. A tangential thought process is often misinterpreted as part of normal aging, but it actually is an indicator of disorganized thinking. Acute onset of cognitive dysfunction over hours to days, impairment of attention, disorganized thinking, and fluctuating mental status are core features of delirium. Increased or decreased psychomotor activity, disorientation, and perceptual disturbances are other supportive features. The use of a screening instrument (such as the Confusion Assessment Method) allows for improved recognition and diagnosis of delirium.

Delirium is an underrecognized disorder in older patients who are hospitalized and may result from various causes, including organ failure (such as the worsening kidney function in this patient), metabolic disturbances, medications, or infection. A key to the likely cause of delirium in this patient is myoclonus seen on physical examination. Myoclonus is a sudden involuntary muscle contraction (positive myoclonus) or sudden brief loss of muscle activity (negative myoclonus, or asterixis); this patient's examination shows asterixis, a common finding in metabolic disturbances (uremia, liver failure, or hypoglycemia) and toxic encephalopathy (due to antibiotics, pain medications, and immunosuppressants).

Although the presence of delirium significantly increases the risk of developing dementia and, conversely, dementia is a significant risk factor for developing delirium, this patient was previously functioning independently. The onset of dementia is typically insidious. The diagnosis of dementia requires 6 months of progressive cognitive decline.

Nonconvulsive status epilepticus (NCSE), or alteration in mental status without overt convulsive activity as a result of continuous or near continuous epileptiform discharges, is often unrecognized in older patients with mental status changes and should be considered as part of the differential diagnosis of acute confusional state if the cause remains unknown. However, the cause of delirium is often identifiable by a careful history, physical examination, and review of medical conditions or interventions that may be contributing to a change in mental status. Additionally, the negative myoclonus seen in this patient would be unlikely in a patient with NCSE without a history of preexisting epilepsy.

Although stroke presents with an abrupt onset, and this patient is at higher risk for stroke because of his recent myocardial infarction, this patient does not have any focal neurologic signs, such as dysarthria, facial droop, hemiparesis, or dysmetria, to suggest that a stroke has occurred.

Question 90

A 49-year-old woman is evaluated for a 1-year history of severe fatigue. She often requires a nap in the middle of the day to continue to function and notes that her work productivity is reduced. The patient has multiple sclerosis (MS), which was diagnosed 2 years ago and is well controlled with daily teriflunomide. Other medications are nightly amitriptyline and weekly vitamin D supplementation.

On physical examination, temperature is 36.9 °C (98.4 °F), blood pressure is 105/64 mm Hg, pulse rate is 68/min, and respiration rate is 14/min; BMI is 21. All other physical examination findings are normal, and neurologic examination findings are unchanged from those obtained at her baseline examination.

Results of laboratory studies show a hemoglobin level of 13.1 g/dL (131 g/L), a mean corpuscular volume of 90 fL, and a serum thyroid-stimulating hormone level of 1.4 μU/mL (1.4 mU/L).

An MRI of the brain obtained 1 month ago as part of routine surveillance showed white matter lesions consistent with MS and unchanged from their appearance 1 year ago.

Which of the following is the most appropriate treatment for this patient?

A

Iron supplementation

B

Levothyroxine

C

Modafinil

D

Nocturnal continuous positive airway pressure

E

Substitution of dimethyl fumarate for teriflunomide

Answer & Critique

Correct Answer: C

Educational Objective: Treat fatigue in multiple sclerosis.

Key Point

Modafinil is often a successful treatment of fatigue in multiple sclerosis.

This patient should be treated with modafinil. She is experiencing fatigue related to her multiple sclerosis (MS). Fatigue is a very common symptom of MS but is often underevaluated and undertreated. Given this patient's decreased work performance and need for daytime sleep, pharmacologic treatment is indicated. The stimulant medications modafinil and armodafinil are frequently used in patients with MS. Amantadine also is an effective therapy for fatigue. For fatigue refractory to these medications, methylphenidate or other amphetamines may be considered.

Iron supplementation is an appropriate treatment for iron deficiency anemia, which can sometimes result in fatigue and always should be excluded as a cause in patients with MS. However, this patient's normal hemoglobin level and normal mean corpuscular volume argue against her being iron deficient.

Although hypothyroidism also can result in fatigue, this patient is clinically euthyroid, and her thyroid-stimulating hormone level is normal. Thyroid hormone supplementation in the absence of hypothyroidism is not appropriate treatment for the fatigue associated with MS.

Nocturnal continuous positive airway pressure (CPAP) can be an appropriate treatment of obstructive sleep apnea (OSA) and other causes of daytime sleepiness, such as primary sleep disorder. OSA should be considered in patients with MS and severe fatigue. However, this patient has no clinical history consistent with OSA, and thus prescribing CPAP without diagnostic polysomnography would not be appropriate.

This patient's history, physical examination, and imaging findings give no indication that her disease-modifying drug is resulting in treatment failure. Therefore, the teriflunomide does not have to be replaced with dimethyl fumarate or any other drug. In addition, fatigue is not a known adverse effect of teriflunomide, and this patient's fatigue is not a sign of medication intolerance

Question 91

A 74-year-old woman is seen for a follow-up evaluation of generalized muscle pain. She first noticed diffuse myalgia 6 months ago; the pain became more severe over the next 2 months, and she began experiencing mild proximal weakness in both upper and lower extremities. Her serum creatine kinase level at that time was 2200 U/L. She was instructed to discontinue the simvastatin she took for hyperlipidemia, and the muscle pain and weakness resolved. The patient also has coronary artery disease treated with aspirin, metoprolol, and isosorbide dinitrate.

On physical examination, blood pressure is 130/80 mm Hg; other vital signs also are normal. No muscle tenderness is noted. All other findings of the general physical and neurologic examinations are normal.

Laboratory studies show a serum creatine kinase level of 250 U/L.

Which of the following is the most appropriate treatment?

A

Atorvastatin

B

Gemfibrozil

C

Rosuvastatin

D

Selenium

Answer & Critique

Correct Answer: C

Educational Objective: Treat statin-related toxic myopathy with a hydrophilic statin.

Key Point

Hydrophilic statins, such as rosuvastatin, are less likely than lipophilic statins to cause statin-induced myopathy.

Rosuvastatin is the most appropriate treatment for this patient with hyperlipidemia. Hydrophilic statins, especially rosuvastatin but also pravastatin and fluvastatin, are less likely than lipophilic statins (such as atorvastatin, simvastatin, and lovastatin) to cause statin-induced myopathy and can be used at low doses in patients with previous statin-related myalgia, myopathy, or mild rhabdomyolysis. Hydrophilic statins also are much less likely than lipophilic statins to cause muscle weakness and elevated serum creatine kinase levels. Lipophilic statins should be avoided in patients with previous statin-related myopathy or rhabdomyolysis. Recently, an immune-mediated necrotizing form of statin myopathy that is associated with anti-HMGCR autoantibodies has been identified in some statin-exposed patients; this form continues to progress even after removal of the statin and may require immunosuppression as treatment. This patient, whose symptoms have resolved after discontinuation of the simvastatin, has no evidence of this type of statin myopathy.

Gemfibrozil is a fibric acid derivative that is typically used for the treatment of hypertriglyceridemia. If added to statin therapy, gemfibrozil raises the serum concentration of statins by twofold, which increases the risk of rhabdomyolysis. Cytochrome P3A4 inhibitors, such as antifungal agents, macrolides, immunophilin ligands, and tricyclic antidepressants, also can increase risk of statin-induced myopathy.

Although selenium supplementation does not treat hyperlipidemia, it has been suggested as a potential method of preventing statin-induced myopathy. Available evidence, however, does not allow a definitive conclusion to be drawn.

Question 92

A 56-year-old man is evaluated for a 5-year history of gradually worsening behavioral problems. During this period, the patient has lost four different jobs because of argumentativeness with his bosses and rudeness toward coworkers and customers. According to his wife, he has become increasingly indifferent toward most things, including his family about whom he used to care deeply; has lost all interest in socializing with friends; and has started to drink excessively. He has become preoccupied with counting change and other belongings and has developed compulsive rituals from which he does not diverge. The patient also has begun collecting scrap metals, an activity he greatly enjoys. He says he does not feel down or hopeless and has not had periods of elation, euphoria, or irritability accompanied by an increased energy level. His memory has remained good. During the interview, the patient states that he has not noticed any change in his behavior and contributes little else to the history. His father was institutionalized for an unknown psychiatric illness at age 55 years.

On physical examination, vital signs are normal. The general physical and neurologic examinations are normal. His score on the Mini–Mental State Examination is 29/30, with one point deducted for orientation to date.

Which of the following is the mos t likely diagnosis?

A

Alzheimer disease

B

Dementia with Lewy bodies

C

Depression

D

Frontotemporal dementia

Answer & Critique

Correct Answer: D

Educational Objective: Diagnose behavioral variant frontotemporal dementia.

Key Point

Behavioral variant frontotemporal dementia is characterized by the typical features of hyperorality, loss of insight, loss of empathy, compulsive behaviors, impaired social conduct, and an early age of onset.

This patient likely has the behavioral variant type of frontotemporal dementia (FTD). This form of FTD is a clinical syndrome characterized by the insidious onset of changes in behavior, personality, and executive function. This patient demonstrates the typical features of hyperorality (as evidenced by excessive alcohol intake), loss of insight, loss of empathy, compulsive behaviors, and impaired social conduct. An early age of onset is typical for the disease. Behavioral variant FTD is the second most common cause of early-onset dementia, second only to Alzheimer disease. A family history of a related neuropsychiatric disorder is evident in approximately 40% of patients with FTD; this patient's family history of a father being institutionalized in his 50s is thus concerning. Patients with behavioral variant FTD typically do well on the Mini–Mental State Examination because executive function is not well assessed by this screening test, and this cognitive domain is most likely to be impaired in patients with FTD.

Although Alzheimer disease is the most common cause of early-onset dementia, the disease presentation in this patient is not typical for this diagnosis. On cognitive testing, patients with Alzheimer disease typically exhibit impairment on tests of learning, memory, and visuospatial function. This patient showed none of these impairments.

This patient's decline in functioning can be attributed to behavioral dysfunction rather than cognitive impairment, which is the cause of impaired functioning in patients with dementia with Lewy bodies. In addition, he lacks other supportive features of dementia with Lewy bodies, such as parkinsonism, formed visual hallucinations, fluctuating cognition, rapid eye movement sleep behavior disorder, or autonomic dysfunction.

Patients with behavioral variant FTD are frequently misdiagnosed with a psychiatric illness, such as depression, bipolar disorder, or another mood or personality disturbance, especially early in the disease course. Although this patient has a few symptoms of depression, such as apathy and loss of interest, the prominent changes in behavior and lack of additional depressive symptoms make behavioral variant FTD the more likely diagnosis.

Question 93

A 58-year-old woman is evaluated for cognitive impairment. The patient was brought to the office by her daughter because of a progressive inability to care for herself and manage her finances over the past 2 months. She also has become more withdrawn, emotionally blunted, and disinterested in former social activities and hobbies. She previously was successfully employed as a substitute teacher. She has no significant medical history and no family history of a neurologic or psychiatric disorder.

On physical examination, vital signs are normal. Neurologic examination shows generalized slowness, but findings are otherwise normal. She scores 10/30 on the Montreal Cognitive Assessment, losing points in all eight sections.

Results of laboratory studies, including a complete blood count, comprehensive metabolic profile, thyroid function tests, vitamin B_{12} level, erythrocyte sedimentation rate, rapid plasma reagin test, HIV antibody titer, and urinalysis, are normal.

A diffusion-weighted MRI of the brain is shown.

Which of the following is the most likely diagnosis?

A

Alzheimer disease

B

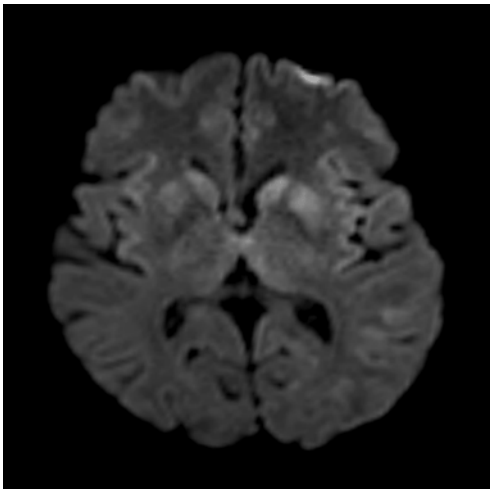
Creutzfeldt-Jakob disease

C

Herpes simplex virus 1 encephalitis

D

Vascular neurocognitive disorder



Answer & Critique

Correct Answer: B

Educational Objective: Diagnose Creutzfeldt-Jakob disease.

Key Point

Creutzfeldt-Jakob disease can be diagnosed by the presence of hyperintensities in the cerebral cortex (cortical ribboning), basal ganglia, or thalamus on diffusion-weighted imaging, which is highly sensitive and specific for the diagnosis.

This patient most likely has Creutzfeldt-Jakob disease (CJD), a dementing illness that occurs subacutely over weeks to months and is classified as a rapidly progressive dementia. This patient has the hallmark neuroradiologic finding of sporadic CJD, namely, hyperintensities on diffusion-weighted imaging (DWI), in this instance involving the basal ganglia and insular and left parietal cortices. DWI hyperintensities also can occur in the cerebral cortex (as cortical ribboning) and thalamus in CJD. DWI is highly sensitive and specific for the diagnosis of sporadic CJD.

Alzheimer disease can present as a rapidly progressive dementia, but not commonly. The MRI findings seen in this patient are not consistent with Alzheimer disease, in which the MRI is typically normal or shows focal atrophy involving the temporal and/or parietal lobes.

Rapidly progressive dementias are relatively uncommon and are more likely to be due to treatable, reversible causes than are the more typical dementing conditions that develop over years. Herpes simplex virus 1 (HSV-1) encephalitis typically results in an acute neurologic decline occurring over days to 1 week rather than months as with this patient. Fever, focal neurologic findings, and focal

seizures are common. T2 hyperintensities (and occasionally DWI hyperintensities), with a predilection for the temporal lobes, are strongly suggestive of HSV-1 encephalitis, rather than the DWI abnormalities seen in this patient.

Vascular neurocognitive disorder is characterized by cognitive impairment occurring after a clinical stroke or in the presence of neuroimaging findings of cerebrovascular disease. The prevalence of poststroke dementia is approximately 30%. This patient has neither the history nor focal neurologic signs (such as hemiparesis, facial droop, or dysarthria) to suggest that a clinical stroke has occurred. Although DWI is very sensitive in the detection of early ischemic infarction, the DWI abnormalities seen in this patient do not follow vascular territories and are instead classic for sporadic CJD.

uestion 94

A 57-year-old man is evaluated in the emergency department 45 minutes after developing acute-onset left arm weakness. He has type 2 diabetes mellitus and a 50-pack-year smoking history. He has no history of stroke, trauma, bleeding, cardiac disease, or surgery. His only medications are atorvastatin and metformin.

On physical examination, blood pressure is 168/98 mm Hg and pulse rate is 86/min and irregular. Neurologic examination reveals left hemineglect, an inferior left visual field deficit, left facial weakness, mild dysarthria, and left arm and leg drift. He scores 6 on the National Institutes of Health Stroke Scale, indicating a moderate stroke.

Laboratory study findings include a plasma glucose level of 162 mg/dL (9.0 mmol/L); results of a complete blood count, a comprehensive metabolic profile, and coagulation studies are normal.

An electrocardiogram shows atrial fibrillation. A noncontrast CT scan of the head shows no acute infarct or hemorrhage.

Which of the following is the most appropriate next step i n treatment?

A

High-dose aspirin

B

Insulin

C

Intravenous heparin

D

Intravenous recombinant tissue plasminogen activator

Answer & Critique

Correct Answer: D

Educational Objective: Treat acute ischemic stroke with thrombolysis.

Key Point

In patients with focal neurologic symptoms suggestive of an acute ischemic stroke, recombinant tissue plasminogen activator should be administered within 3 hours of symptom onset to patients who do not meet any of the exclusion criteria.

This patient should receive intravenous recombinant tissue plasminogen activator (rtPA). He is within the 3-hour window for treatment of patients who do not meet any of the exclusion criteria for thrombolysis. In the National Institute of Neurological Diseases and Stroke (NINDS) rtPA trial, patients who received intravenous rtPA within 3 hours of stroke onset had a greater likelihood of clinical improvement at 3 months compared with those who received placebo. The trial included patients with atrial fibrillation and all ischemic stroke subtypes and showed no significant safety difference between stroke subtypes. Because he has no contraindications to thrombolysis, it is the treatment of choice in this patient.

High-dose (325-mg) aspirin would be an appropriate initial treatment if the patient met any of the exclusion criteria for thrombolysis, which he does not. As long as a follow-up CT scan of the head shows no hemorrhage, aspirin should be initiated 24 hours after administration of rtPA.

Hyperglycemia is common in patients with acute ischemic stroke and, if persistent in the first 24 hours after stroke onset, is associated with poor functional outcomes. To date, no definitive clinical trials have outlined the best approach to treatment or the most appropriate targets. Acute ischemic stroke guidelines are thus in keeping with general recommendations for all critically ill hospitalized patients who have mild hypertension, with or without diabetes mellitus, which are not to use intensive insulin therapy to normalize plasma glucose levels. If insulin therapy is required, the American College of Physicians recommends target plasma glucose levels of 140 mg/dL to 200 mg/dL (7.8-11.1 mmol/L) while monitoring carefully for hypoglycemia. Insulin therapy is thus not indicated in this patient whose plasma glucose level falls in the target range.

Intravenous heparin does not reduce the 14-day risk of recurrent stroke or mortality in patients with atrial fibrillation who have a new stroke and is therefore not indicated.

Question 95

A 55-year-old man is treated in the emergency department for convulsive status epilepticus. He stops convulsing after receiving intravenous lorazepam and phenytoin but is still confused 30 minutes after treatment. According to his wife who accompanied him, a left temporal cavernous malformation was detected 3 years ago and has been managed conservatively. He has no significant family medical history and takes no chronic medication.

On physical examination, temperature is 36.8 °C (98.2 °F), blood pressure is 130/90 mm Hg, pulse rate is 115/min, and respiration rate is 12/min. The patient is generally stuporous but intermittently alert to voice or sternal rub. He occasionally utters nonsensical phrases, mostly consisting of syllables that are not real words, and inconsistently follows some one-step commands. Cranial nerves are intact, and pupils are symmetric and reactive. No weakness is detected in the face or limbs.

A CT of the head shows an acute hemorrhage in the region of the patient's cavernous malformation. The hemorrhage measures 0.5 × 0.5 × 1.0 cm. No significant mass effect or midline shift is noted.

Which of the following is the most appropriate next step in management?

A

Continuous electroencephalographic monitoring

B

Intravenous flumazenil

C

Urgent surgical resection of the vascular malformation

D

Withholding of further doses of antiepileptic drugs

Answer & Critique

Correct Answer: A

Educational Objective: Diagnose nonconvulsive status epilepticus with continuous electroencephalographic monitoring.

Key Point

All patients with altered mental status after convulsive status epilepticus should have continuous electroencephalographic monitoring for at least 24 hours to detect nonconvulsive seizures.

This patient should have continuous monitoring with electroencephalography (EEG) because his presentation is concerning for nonconvulsive status epilepticus (NCSE). Approximately 48% of patients treated for convulsive status epilepticus (CSE) will continue to have subtle or subclinical seizures on EEG. Persistently altered mental status, particularly with waxing and waning features and focal neurologic deficits (such as aphasia), is a characteristic feature of NCSE. Patients with intracranial structural abnormalities who are comatose also are at high risk for this disorder. Intracerebral hemorrhage is an additional risk factor for nonconvulsive seizures and status epilepticus.

Continuous EEG monitoring is twice as sensitive as a routine 30-minute EEG for detecting seizures, especially the intermittent seizures that are common in patients already treated for CSE. All patients with altered mental status after CSE should have continuous EEG monitoring for at least 24 hours to detect nonconvulsive seizures or a changed status. Comatose patients should be evaluated for 24 to 48 hours. Continuous EEG monitoring is indicated in patients with acute structural intracranial lesions and altered mental status, even if clinically evident seizures have not occurred.

Flumazenil should not be administered to any patient with seizures or at risk for seizures because the drug can precipitate status epilepticus. Because the patient is not showing any signs of respiratory depression or other adverse effects of medication, there is no urgent need to reverse the benzodiazepine he received as part of appropriate CSE treatment.

Cavernous malformations usually have self-limited bleeding, and this patient does not have any mass effect or other urgent need for surgery. Although he ultimately may be a surgical candidate,

given that refractory seizures are associated with cavernous malformations, surgical resection is not the most appropriate next step. He first should be evaluated and treated for NCSE.

Maintenance antiepileptic drugs (AEDs) should not be withheld in a patient with CSE at presentation unless the drugs are clearly causing severe adverse effects. In this patient, NCSE is a more likely explanation of the patient's mental state than is an adverse effect of the AED.

Question 96

A 65-year-old woman is admitted to the hospital for evaluation of acute kidney injury secondary to dehydration after an episode of severe gastroenteritis. She has type 1 diabetes mellitus, secondary progressive multiple sclerosis, and osteopenia. Medications are irbesartan, insulin glargine, insulin lispro, glatiramer acetate, dalfampridine, baclofen, vitamin D, and calcium.

On physical examination, temperature is normal, blood pressure is 110/60 mm Hg, pulse rate is 108/min, and respiration rate is 14/min. She appears weak and tired. Neck veins are flat. The remainder of the physical examination is normal.

Results of laboratory studies show a serum creatinine level of 3.9 mg/dL (345 μmol/L), which is increased from her baseline level of 1.4 mg/dL (124 μmol/L).

Intravenous fluids are initiated.

In addition to irbesartan, which of the following medications must be discontinued?

A

Baclofen

B

Dalfampridine

C

Glatiramer acetate

D

Vitamin D

Answer & Critique

Correct Answer: B

Educational Objective: Anticipate the potential adverse effects of medications used for symptomatic treatment of patients with multiple sclerosis.

Key Point

Dalfampridine is renally excreted and thus is contraindicated in patients with kidney disease.

This patient's dalfampridine (4-aminopyridine) should be discontinued. Dalfampridine is a voltage-gated potassium channel antagonist that can potentiate action potentials along demyelinated axons and is used in patients with multiple sclerosis (MS) for potassium channel blockade. This medication can improve lower extremity function and walking speed and endurance. Because of its mechanism of action, seizures have been reported as a rare, dose-dependent adverse effect of this medication. Dalfampridine is excreted through the kidneys and thus is contraindicated in patients with kidney disease because its resultant decreased clearance would significantly increase the seizure risk. For this reason, this medication should be discontinued in this patient.

Baclofen can alleviate the spasticity often associated with MS. There is no reason to discontinue the drug in this patient with acute kidney injury because no specific adverse effects of this drug due to kidney toxicity or related to kidney clearance have been reported. Dosing may have to be modified in patients with severe kidney failure, however.

Glatiramer acetate is a disease-modifying medication used in the treatment of MS to impede disease activity and prevent relapses. This drug has no known adverse effects on the kidneys due to poor clearance or direct toxicity.

Vitamin D supplementation is now suggested for all patients with MS to reduce the accumulation of new lesions on MRI. No adverse effects on kidney function or kidney clearance have been reported.

Bibliography