Practice file

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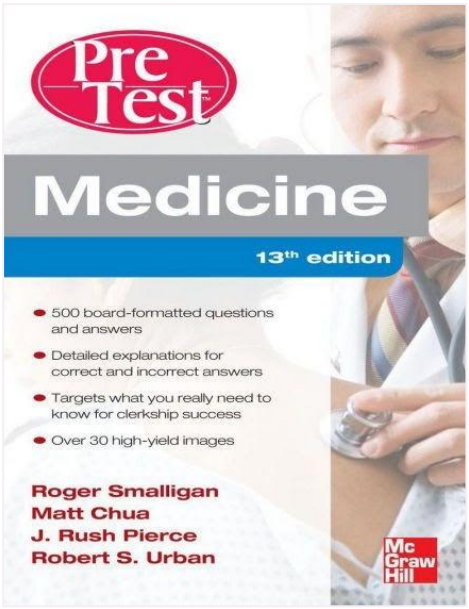
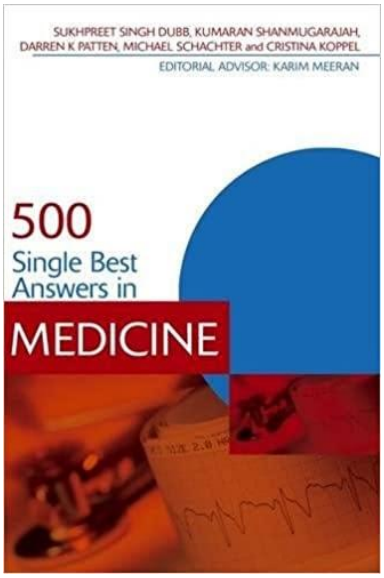
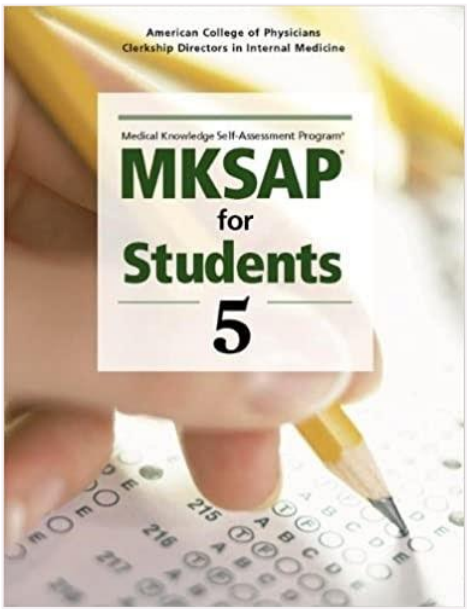






AMBOSS
medical knowledge distilled

Table of content

CNS infections

Q1 (500Best): A 28-year-old junior doctor has been complaining of a headache for the last 24 hours. It started gradually, intensifying slowly and involving the entire cranium, but over the last couple of hours she has noticed that turning her head is uncomfortable. She feels generally unwell and prefers to lie in a dark room. Her boyfriend has noticed that she seems irritable. On examination, she exhibits photophobia and there is neck stiffness. There is no papilloedema. Close examination of her skin reveals no rashes. Kernig's sign is negative. A lumbar puncture (LP) reveals low protein, normal glucose and lymphocytosis. What is the diagnosis?

A- Viral meningitis
B- Migraine
C- Aseptic meningitis
D- Bacterial meningitis
E- TB meningitis

	In essence	Cells	Protein	Glucose
Bacterial	Low glucose, neutrophilia	Neutrophils	↑/N	↓
Viral	High protein, lymphocytosis	Lymphocytes	↑↑N	
TB/fungal	Low glucose, lymphocytosis	Lymphocytes	↑/N	↓
SAH	High RBC	RBC	++	++
		Some WBC	↑/N	N

Explanation: This is clearly a picture of meningitis. Although migraine (B) results in headache associated with photophobia and irritability, the overall picture with abnormal LP along with neck stiffness suggests meningitis. Basic signs of meningitis that you should always look for include: photophobia, neck stiffness, Kernig's sign (patient's leg is held flexed at the hip and knee and there is pain and resistance on subsequent knee extension – not particularly sensitive but useful if present). The analysis of cerebrospinal fluid (CSF) is very helpful in its diagnosis, although the history and clinical picture give a good indication. Viral meningitis is much less severe than bacterial meningitis which can progress rapidly to septicaemia and its complications (signs include septic shock: hypotension and tachycardia, reduced urine output, vasodilatation and a non-blanching petechial rash – you will not find it unless you look for it). If bacterial meningitis is a possibility, antibiotics should be given as soon as possible while the exact diagnosis is made. TB meningitis tends to be more indolent and there may be a history of exposure. The CSF results below give it away:

Q2 (MKSAP): A 19-year-old-woman who is a sophomore in college is evaluated in December for a 24-hour history of fever and headache. She lives in a dormitory on campus. Her medical history is unremarkable. She takes no medications and is up to date with all of her immunizations, including the meningococcal vaccine, which she received before entering college. Two cases of meningococcal serogroup B-associated meningitis have been reported on campus. On physical examination, the patient appears ill. Temperature is 39.1°C (102.4°F), blood pressure is 95/50 mm Hg, pulse rate is 125/min, and respiration rate is 25/min. A purpuric rash is appreciated over both lower extremities. Neck stiffness is present and jolt accentuation of the headache is elicited. A noncontrast CT scan of the head is normal. The leukocyte count is 19,500/µL (19.5 × 109/L) with 87% neutrophils and 13% lymphocytes; platelet count is 110,000/µL (110 × 109/L). Cerebrospinal fluid (CSF) leukocyte count is 2000/µL (2000 × 106/L), with 95% neutrophils and 5% lymphocytes; glucose level is 20 mg/dL (1.1 mmol/L); and protein level is 100 mg/dL (1000 mg/L). The CSF Gram stain reveals gram-negative diplococci. Which of the following is the most likely diagnosis?

A- Neisseria meningitidis meningitis
B- Rocky Mountain spotted fever
C- Streptococcus pneumoniae meningitis
D- Vibrio vulnificus meningitis

Explanation: This patient's illness, physical examination, and CSF profile are consistent with N. meningitidis meningitis. This infection most commonly occurs in children and young adults. The Centers for Disease Control and Prevention (CDC) recommends routine immunization with the meningococcal vaccine, which protects against serogroups A, C, Y, and W-135, but not serogroup B, the causative agent in as many as one third of U.S. cases and the recent cause of other cases of meningitis on campus. Rocky Mountain spotted fever (RMSF) can manifest as headache, fever, myalgia, abdominal pain, and rash. The purpuric rash typically develops 3 to 4 days after the onset of constitutional symptoms and begins on the wrists and ankles before spreading centripetally. Thrombocytopenia, a relative leukopenia, and elevated transaminases may provide clues to the diagnosis, particularly if the patient resides or has traveled to areas where RMSF-associated American dog ticks are present. These ticks transmit infection in spring and early summer but not in December, which is when this patient became ill. Streptococcus pneumoniae is the most common cause of bacterial meningitis in adults. The clinical presentation of pneumococcal meningitis is not specific, but CSF and, possibly, blood cultures will reveal gram-positive (not gram-negative) diplococci. Vibrio vulnificus is a gram-negative bacillus that can cause septicemia, wound infection, and, rarely, gastroenteritis. Wound infection typically occurs by inoculation through the skin, and septicemia and gastroenteritis occurs after ingestion of raw or undercooked shellfish. Invasive disease typically occurs in immunocompromised hosts, particularly those with liver disease. These infections are more common in summer months when warmer sea water temperatures support the growth of this organism. Meningitis is not characteristic of infection with this organism.

Answers: Q1: A | Q2: A

CNS infections

Q3 (MKSAP): A 65-year-old woman is evaluated for a 1-day history of fever, headache, and altered mental status. Medical history includes type 2 diabetes mellitus and hypertension treated with glipizide and hydrochlorothiazide. She has no allergies. On physical examination, the patient is confused. Temperature is 38.9°C (102.0°F), blood pressure is 104/66 mm Hg, pulse rate is 100/min, and respiration rate is 20/min. Her neck is supple, and she has no rashes. The leukocyte count is 19,000/μL (19 × 109/L); platelet count, 90,000/μL (90 × 109/L); and plasma glucose level, 120 mg/dL (6.7 mmol/L). A non-contrast-enhanced CT scan of the head is normal. Cerebrospinal fluid (CSF) analysis shows a leukocyte count of 1300/μL (1300 × 106/L) with 98% neutrophils, a glucose level of 20 mg/dL (1.1 mmol/L), and a protein level of 200 mg/dL (2000 mg/L). CSF Gram stain results are negative for any organisms. Dexamethasone is begun.
Which of the following antimicrobial regimens should now be initiated?

A- Ceftriaxone
B- Penicillin G
C- Vancomycin, ampicillin, and ceftriaxone
D- Vancomycin plus ceftriaxone
E- Vancomycin plus trimethoprim-sulfamethoxazole

Explanation: This patient most likely has bacterial meningitis and requires therapy with vancomycin, ampicillin, and ceftriaxone. Bacterial meningitis in adults is characterized by fever, headache, nuchal rigidity, and signs of cerebral dysfunction. In elderly patients, such as this one, insidious onset with lethargy or obtundation and variable signs of meningeal irritation may be present, particularly in the setting of diabetes mellitus. This patient's symptoms and cerebrospinal fluid results are consistent with acute bacterial meningitis. The most likely etiologic agents are Streptococcus pneumoniae, Listeria monocytogenes, Neisseria meningitidis, and aerobic gram-negative bacilli. Pending culture results and results of in vitro susceptibility testing, empiric treatment with antimicrobial therapy consisting of vancomycin, ampicillin, and ceftriaxone for infection caused by penicillin- resistant pneumococci and L. monocytogenes is necessary. Administration of adjunctive dexamethasone should be strongly considered in patients with acute bacterial meningitis because clinical trials have established the benefit of adjunctive dexamethasone on adverse outcomes and death in adults with suspected or proven S. pneumoniae meningitis. Intravenous ceftriaxone or intravenous penicillin G alone might not provide adequate cerebrospinal fluid levels for treatment of penicillin-resistant S. pneumoniae. Most infectious disease experts would recommend vancomycin plus ceftriaxone for the treatment of penicillin-resistant S. pneumoniae; however, this combination would not adequately treat meningitis caused by L. monocytogenes, which requires the addition of ampicillin. Trimethoprim-sulfamethoxazole does treat Listeria meningitis, but the combination of vancomycin plus trimethoprim-sulfamethoxazole would be potentially inadequate treatment for S. pneumoniae meningitis.

Q4 (pretest): A 52-year-old previously healthy woman presents with behavioral abnormalities and aphasia. Her husband reports that her symptoms began 3 days ago with fever and headache. On examination, she has a temperature of 38.4°C (101°F), mild nuchal rigidity, and agitation. When questioned, she repeats the question or responds with nonsense words. CT scan shows mild temporal hypodensity on the right; CSF examination shows 354 WBC with 75% lymphocytes. The CSF protein is elevated at 167 mg/dL, but the CSF glucose is normal at 112 (simultaneous peripheral glucose 142).

A- Pneumococcal meningitis
B- Cryptococcal meningitis
C- Coxsackievirus (aseptic) meningitis
D- Listeria monocytogenes meningitis
E- Herpes simplex encephalitis

Explanation: CSF infections can present with meningeal inflammation, parenchymal involvement, or both. The patient has both meningitis (fever, nuchal rigidity, CSF pleocytosis) and focal brain involvement (temporal lobe signs). The combination of high lymphocyte count in the CSF with cortical brain dysfunction indicates encephalitis. The most common cause of sporadic (ie, nonepidemic) encephalitis is herpes simplex encephalitis; prompt diagnosis and treatment with intravenous acyclovir can decrease permanent brain damage and improve survival. The commonest cause of seasonal encephalitis in the United States is now West Nile virus infection. Viral (aseptic) meningitis causes a similar lymphocytic pleocytosis with normal CSF glucose level but is not associated with brain dysfunction such as confusion, aphasia, ataxia, or focal weakness.

Answers: Q3: C | Q4: E

CNS infections

Q5 (AMBOSS): A 13-year-old girl is brought to the physician because of worsening fever, headache, photophobia, and nausea for 2 days. One week ago, she returned from summer camp. She has received all age-appropriate immunizations. Her temperature is 39.1°C (102.3°F). She is oriented to person, place, and time. Physical examination shows a maculopapular rash. There is rigidity of the neck; forced flexion of the neck results in involuntary flexion of the knees and hips. Cerebrospinal fluid studies show:

A- Mumps virus
B- Echovirus
C- Listeria monocytogenes
D- Herpes simplex virus
E- Streptococcus pneumoniae

Opening pressure	120 mm H_2O
Appearance	Clear
Protein	47 mg/dL
Glucose	68 mg/dL
White cell count	280/mm^3
Segmented neutrophils	15%
Lymphocytes	85%

Explanation: Echovirus and other enteroviruses are typically responsible for summer outbreaks of aseptic meningitis, especially in children and teenagers. Enteroviruses are the most common cause of aseptic meningitis overall. Aseptic meningitis commonly manifests with a nonspecific rash, fever, headache, nuchal rigidity, and a positive Brudzinski sign.

Q6 (AMBOSS): A previously healthy 1-year-old boy is brought to the emergency department because of irritability and fever for 2 days. His symptoms began shortly after returning from a family trip to Canada. He was born at term. His immunizations are up-to-date. His 6-year-old brother is healthy and there is no family history of serious illness. The boy appears weak and lethargic. He is at the 50th percentile for height and 75th percentile for weight. His temperature is 39.2°C (102.5°F), pulse is 110/min, respirations are 28/min, and blood pressure is 92/55 mm Hg. Physical examination shows several purple spots over the trunk and extremities that are 1 mm in diameter. Capillary refill time is 4 seconds. The remainder of the examination shows no abnormalities. His hemoglobin concentration is 12 g/dL, leukocyte count is 19,000/mm3, and platelet count is 225,000/mm3. A lumbar puncture is done; cerebrospinal fluid analysis shows abundant segmented neutrophils, decreased glucose concentration, and an increased protein concentration. Which of the following is the most appropriate next step in management?

A- Cefotaxime and vancomycin therapy for the patient and doxycycline prophylaxis for close contacts
B- Cefotaxime and vancomycin therapy for the patient and no prophylaxis for close contacts
C- Ampicillin therapy for the patient and ciprofloxacin prophylaxis for close contacts
D- Ceftriaxone and vancomycin therapy for the patient and rifampin prophylaxis for close contacts
E- Vancomycin therapy for the patient and rifampin prophylaxis for close contacts

Explanation: A combination of vancomycin and a third-generation cephalosporin (ceftriaxone, cefotaxime) is used for empiric treatment of community-acquired meningitis to cover the most likely pathogens in patients between 1 month and 50 years of age, including S. pneumoniae, N. meningitidis, and H. influenza. Meningococcal meningitis has a high case fatality rate (up to 13%). Rifampin is indicated for PEP in all close contacts (i.e., the patient's brother and parents). PEP is important to prevent infection, and to eliminate nasopharyngeal carriage of N. meningitidis, thus limiting disease transmission.

Ceftriaxone should be avoided in patients < 1 month of age because of an increased risk of biliary sludging and kernicterus.

Q7 (AMBOSS): A 61-year-old man is brought to the emergency department because of a 2-day history of fever, chills, and headache. He frequently has headaches, for which he takes aspirin, but says that this headache is more intense. His wife reports that he has also not been responding right away to her. He has a 20-year history of hypertension and poorly controlled type 2 diabetes mellitus. His current medications include metformin and lisinopril. He has received all recommended childhood vaccines. His temperature is 39°C (102.2F°), pulse is 100/min, and blood pressure is 150/80 mm Hg. He is lethargic but oriented to person, place, and time. Examination shows severe neck rigidity with limited active and passive range of motion. Blood cultures are obtained and a lumbar puncture is performed. Which of the following is the most likely causal organism?

A- Neisseria meningitidis
B- Listeria monocytogenes
C- Streptococcus pneumoniae
D- Pseudomonas aeruginosa

Explanation: Streptococcus pneumoniae is the single most common cause of bacterial meningitis among adults of all ages in the US, accounting for over half of all reported cases. Streptococcus pneumoniae is also the most common cause of community-acquired bacterial meningitis in diabetic patients despite the fact that diabetes increases the risk of meningitis caused by other bacteria.

Answers: Q5: B | Q6: D | Q7: C

CNS infections

Q8 (AMBOSS): A 45-year-old man comes to the emergency department with a 3-day history of progressively worsening headache and nausea. He started having chills last night and could not fall asleep. He has not had any vomiting or diarrhea. He has a history of hypertension treated with ramipril. He works 80 hours per week as an investment banker and says that his job is stressful. He is sexually active with several female partners and uses condoms consistently. He drinks alcohol occasionally on the weekends and does not smoke or use illicit drugs. His immunizations are up-to-date. He appears exhausted. He is oriented to place and person but not to time. He becomes increasingly somnolent as one of the nurses takes his vital signs. His temperature is 39.5°C (103.1°F), pulse is 67/min, respirations are 17/min, and blood pressure is 127/77 mm Hg. Physical examination shows photophobia and nuchal rigidity; Kernig and Brudzinski signs are present. Fundoscopic examination shows no abnormalities. Blood samples are obtained for cultures and therapy with vancomycin and cefotaxime is initiated. Which of the following is the most appropriate next step in diagnosis?

A- CT scan of the head
B- Lumbar puncture
C- MRI of the head
D- Cerebral arteriography
E- Electroencephalography

Explanation: CT scan of the head before lumbar puncture (LP) is indicated in patients presenting with typical signs of acute meningitis accompanied by signs of increased intracranial pressure or a mass lesion (e.g., altered mental status). The primary goal of obtaining neuroimaging before LP is to mitigate the risk of brain herniation, which can be precipitated by the transient decrease in intracranial pressure caused by LP. This patient is somnolent and oriented only to place and person and therefore meets the criteria for neuroimaging before an LP. Indications for performing a head CT prior to LP in patients with suspected meningitis are summarized in the mnemonic "FAILS:" Focal neurological deficit, Altered mental status, Immunocompromised/ICP elevated, Lesion in the brain or skin near LP site, new-onset Seizures.

The presence of papilledema has high specificity but low sensitivity for the diagnosis of increased intracranial pressure (ICP), which means that a normal fundoscopic examination, as seen here, is not sufficient to rule out elevated ICP.

Q9 (AMBOSS): A 16-day-old male newborn is brought to the emergency department because of fever and poor feeding for 2 days. He became very fussy the previous evening and cried for most of the night. He was born at 36 weeks' gestation and weighed 2430 g (5 lb 3 oz). The pregnancy and delivery were uncomplicated. The mother does not recall any sick contacts at home. He currently weighs 2776 g (6 lb 2 oz). He appears irritable. His temperature is 38.6°C (101.5°F), pulse is 180/min, and blood pressure is 82/51 mm Hg. Examination shows scleral icterus. He becomes more agitated when picked up. There is full range of motion of his neck and extremities. The anterior fontanelle feels soft and flat. Neurologic examination shows no abnormalities. Blood cultures are drawn and fluid resuscitation is initiated. A urinalysis obtained by catheterization shows no abnormalities. Which of the following is the most appropriate next step in diagnosis?

A- MRI of the head
B- Urine culture
C- Lumbar puncture
D- CT scan of the head
E- X-ray of the chest

Explanation: A lumbar puncture should be performed in all clinically stable neonates with suspected meningitis or signs of sepsis and no signs of increased intracranial pressure. In neonates, meningitis often manifests with nonspecific symptoms and without the classic triad of meningitis. CSF analysis can confirm the diagnosis and guide antibiotic treatment. Until the results of the CSF analysis are available, patients should be treated with empiric antibiotic therapy (e.g., ampicillin plus gentamicin and/or cefotaxime in patients < 1-month).

In patients with signs of increased intracranial pressure (e.g., seizures), imaging should be obtained before performing a lumbar puncture. In neonates and infants, a cranial ultrasound is usually the preferred method of neuroimaging. In older children, a CT scan should be performed. Although a bulging fontanelle can be a sign of increased intracranial pressure, it is not an indication for imaging on its own.

Answers: Q8: A | Q9: C

Ischemic stroke

Q1 (500Best): A 79-year-old man is admitted with left hemiparesis. CT reveals a middle cerebral artery infarct. What is his most significant risk factor for stroke?

A- Hypertension
B- Smoking
C- Family history
D- Diabetes
E- Cholesterol

Explanation: The three most important risk factors for stroke are hypertension, hypertension and hypertension (A)! INTERSTROKE, a recent large case–control study evaluating risk factors for stroke, has shown that ten risk factors are associated with 90 per cent of the risk of stroke and that of these modifiable risk factors, hypertension is the most important for all stroke subtypes and is a particularly dangerous risk factor for intracerebral haemorrhage. Other risk factors include smoking (B), lipids (E) and diabetes (D) which promote atherosclerosis. Poor diet, lack of regular activity and increased waist–hip ratio are as significant risk factors as smoking. Unmodifiable risk factors include increasing age (by far the most significant), male sex, family history (C) and ethnicity (higher in Blacks and Asians). Patients in atrial fibrillation have an annual stroke risk of 5 per cent. This can be lowered to 1 per cent by anticoagulating with warfarin, aiming for an international normalized ratio (INR) of between 2 and 3 (avoid confusion with aspirin which is an antiplatelet). Stroke is the third most common cause of death in England (after heart disease and cancer) and is more often disabling than fatal, so primary and secondary prevention are crucial.

Q2 (500Best): A 71-year-old right-handed male is brought in by ambulance at 17:50 having suffered a collapse. His wife came home to find him on the floor unable to move his right arm or leg and unable to speak. Her call to the ambulance was logged at 17:30. He has a past medical history of well-controlled hypertension, ischaemic heart disease and atrial fibrillation for which he is on warfarin. He had a hernia repair three months ago and his brother had a 'bleed in the brain' at the age of 67. What is the absolute contraindication to thrombolysis in this male?

A- Family history of haemorrhagic stroke
B- History of recent surgery
C- Time of onset
D- Current haemorrhagic stroke
E- Warfarin treatment

Explanation: This man presents with a stroke. It is clinically impossible to tell with certainty whether it is ischaemic or haemorrhagic (D) which is why he needs a CT to differentiate between the two. However, the time of onset is unclear and therefore it is not possible to determine whether he is outside the 3-hour time window for thrombolysis (C). Neither warfarin treatment (E) nor family history of haemorrhagic stroke (A) are absolute contraindications although they would be taken into consideration. INR should be <1.7. The absolute contraindications for thrombolysis are: onset of symptoms more than 3 hours ago, seizures at presentation, uncontrolled blood pressure (over 180/110), previous intracranial bleed, lumbar puncture in the last week, ischaemic stroke or head injury in the last three months, active bleeding (not menstruation), surgery (B) or major trauma (including CPR) within the last 2 weeks or non-compressible arterial puncture within the last week.

Q3 (500Best): A 77-year-old woman is admitted to hospital with a urinary tract infection. She receives antibiotics and seems to be responding well. On the fourth day she is eating her lunch when she suddenly drops her fork. She calls for the nurse who notices the left side of her face is drooping. What is the best next course of action?

A- CT head
B- Thrombolysis
C- MRI head
D- Aspirin
E- Place nil by mouth

Explanation: This patient has suffered a stroke. This is a medical emergency. As she is within the 3-hour window for thrombolysis (B), she must be assessed immediately. However, thrombolysis is only useful in ischaemic stroke and can severely worsen haemorrhagic stroke. It is impossible to clinically tell the difference with certainty; she therefore warrants urgent imaging. Haemorrhages are much easier to detect on CT (A) as blood shows up white (hyperdense), plus there is easier access to CT unlike MRI (C) which is not always available. If thrombolysis is contraindicated, 300 mg of aspirin (D) is given in the case of ischaemic stroke. Option (E), however, is the most appropriate next step as removing her lunch is a quick, simple intervention that may prevent the complication of aspiration pneumonia. The nurse can then call the doctors or put out a thrombolysis call.

Answers: Q1: A | Q2: C | Q3: E

Ischemic stroke

Q4 (500Best): On observation, a patient has a left facial droop. On closer examination his nasolabial fold is flattened. When asked to smile, the left corner of his mouth droops. He is unable to keep his cheeks puffed out. Eye closure is only slightly weaker compared to the right and his forehead wrinkles when he is asked to look up high. What is the diagnosis?

A- Right middle cerebral artery stroke
B- Parotid gland tumour
C- Left internal capsule stroke
D- Bell's palsy
E- Cerebellar pontine angle tumour

Explanation: The patient presents with a CN VII (facial) palsy. The key feature here is forehead sparing which implies an upper motor neuron lesion. This excludes Bell's palsy (D) and parotid gland (B) or cerebellar pontine angle (CPA) tumours (E) as these would affect the lower motor neuron. In the case of CPA tumours, there is likely to be cerebellar, CN V and CN VIII involvement too. The most common cause of a lower motor neuron CN VII palsy is Bell's palsy which is idiopathic and a diagnosis of exclusion. It is treated conservatively with lubricating eye drops and taping down the eye at night to avoid corneal ulcers. Medically, steroids should be given within 48 hours of onset along with acyclovir. Most patients will recover, although around 10 per cent may be left with permanent deficits. An upper motor neuron facial palsy is most commonly due to stroke. In this case, the left- sided symptoms point to a right hemisphere lesion (A, and not C).

Q5 (500Best): A patient is admitted with a stroke. On examination of her visual fields, she is unable to see in the right lower quadrant of her field. Where is the lesion?

A- Optic chiasm
B- Left parietal lobe
C- Right temporal lobe
D- Right optic radiation
E- Left optic nerve

Explanation: A lesion in the left parietal lobe (B) results in a right lower quadrantanopia. Quadrantanopias and hemianopias are contralateral to the lesion. Temporal (C) and parietal lesions result in upper and lower quadrantanopias, respectively. Complete optic radiation lesions (D) result in hemianopia. Lesions at the optic chiasm (A), such as pituitary tumours and craniopharyngeomas, result in a bitemporal hemianopia. Optic nerve lesions (E) result in ipsilateral monocular visual loss. Note: when laterality is mentioned, always clarify contra/ipsilateral to what, e.g. the signs, the lesion.

Q6 (MKSAP): A 74-year-old man is brought to the emergency department by ambulance 1 hour after he had an acute witnessed onset of aphasia and right hemiparesis. He has a history of hypertension. His current medications are hydrochlorothiazide and metoprolol. On physical examination, blood pressure is 178/94 mm Hg and pulse rate is 80/min and regular. Neurologic examination confirms nonfluent aphasia, a right pronator drift, a right leg drift, and an extensor plantar response on the right. An electrocardiogram obtained on the patient's arrival at the emergency department documents sinus rhythm. A CT scan of the head obtained within 1 hour of his arrival reveals early ischemic changes. Which of the following is the best treatment?

A- Aspirin
B- Continuous intravenous heparin
C- Intravenous labetalol
D- Intravenous recombinant tissue plasminogen activator

Explanation: This patient should receive intravenous recombinant tissue plasminogen activator (rtPA). He has clinical symptoms and signs and radiologic evidence of an acute left hemispheric stroke. The probable mechanism of stroke is ischemic infarction, given the results of the head CT scan. He was brought to the emergency department within 1 hour of the witnessed onset of stroke symptoms, and his evaluation is completed 1 hour later. He does not appear to have any clinical, radiologic, or laboratory contraindication to receiving the preferred treatment of intravenous rtPA, and he can receive it within the recommended window of 3 hours from stroke onset.Aspirin is indicated for acute ischemic stroke in patients who are not eligible for rtPA. For patients with acute stroke who are eligible for thrombolysis, aspirin should be withheld in the emergency department and for 24 hours after rtPA administration. Although long-term anticoagulation is an effective treatment for prevention of cardioembolic stroke in patients with atrial fibrillation, acute anticoagulation with heparin has not been shown to be beneficial in patients with acute ischemic stroke.

Answers: Q4: A | Q5: B | Q6: D

Ischemic stroke

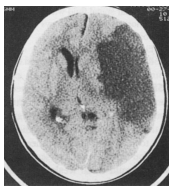
Q7 (pretest): A 65-year-old man presents with right-sided weakness and expressive aphasia that began suddenly 2 hours ago. He has a history of osteoarthritis, gout, and hypertension. He has no history of recent head trauma or surgery. Medications include lisinopril, allopurinol, and acetaminophen. On physical examination the patient is alert. His blood pressure is 164/90 and his pulse rate is 66. He has a dense right hemiparesis and is not able to speak. Complete blood count, platelet count, prothrombin time, glucose, and ECG are normal. CT of the head without IV contrast is normal. What is the next best step?

A. Urgent carotid ultrasonography
B. Anticoagulation with heparin
C. Discuss with patient and his family the risks and benefits of intravenous recombinant tissue-type plasminogen activator
D. Aspirin 81 mg orally now
E. MRI scan of the brain

Explanation: This patient presents with a major left middle cerebral artery territory stroke. Patients who present within 3 to 4½ hours of onset of symptoms of ischemic stroke are candidates for thrombolysis, which has been shown to improve disability and decrease long-term neurologic deficit. In one study, 50% of patients treated with recombinant tissue-type plasminogen activator (rtPA) had little or no neurologic deficit 6 months after the stroke, compared to 35% of controls. rtPA is contra- indicated in hemorrhagic strokes. Thus all patients who are candidates should have CT imaging to exclude a hemorrhagic stroke. CT scanning in acute ischemic stroke is frequently normal (as in this patient) and thus the diagnosis of stroke is made on clinical grounds. rtPA use in acute ischemic stroke is associated with a 6% risk of intracranial hemorrhage, which is fatal in 50% of these patients; thus patients and/or their families should be carefully informed of the relative risks and benefits. Patients with intracranial hemorrhage on imaging, recent head trauma (within the past 90 days), surgery within the past 2 weeks, uncontrolled hypertension, coagulopathy, or who present with seizures are not candidates for rtPA. Aspirin and heparin are to be avoided for 24 hours in patients who are given tPA. Extracranial cerebrovascular disease can be diagnosed with carotid ultrasonography, but carotid artery surgery is done to prevent a subsequent stroke and thus carotid ultrasonography can be done nonurgently. MRI scanning is more sensitive for diagnosing acute stroke, but does not need to be done to confirm a stroke in this patient who has clear-cut ischemic findings. MRI scanning is more time- consuming than CT and might put this patient outside the time window for benefit from rtPA.

Q8 (pretest): A 68-year-old man with a history of hypertension and coronary artery disease presents with right-sided weakness, sensory loss, and an expressive aphasia. Symptoms began 6 hours prior to arrival in the ED. Neuroimaging studies are shown in the following figure. In the emergency department the patient's blood pressure is persistently 180/95. Which of the following is the best next step in management of this patient's blood pressure?

A. Administer IV nitroprusside
B. Administer clonidine 0.1 mg po until the blood pressure drops below 140/90
C. Observe the blood pressure
D. Administer IV mannitol
E. Administer IV labetalol



Explanation: Although hypertension is an important cause of stroke, it should not be aggressively treated in the setting of acute cerebral ischemia. Since cerebral autoregulation is disrupted in acute stroke, a drop in blood pressure can decrease perfusion and worsen the so-called ischemic penumbra. Generally, blood pressure elevation up to 220/120 is tolerated. If the patient were a candidate for thrombolytic therapy, it would be acceptable to lower the BP to less than 185/110 with labetalol or nicardipine. Since this patient's symptoms began 6 hours ago, however, he is not a candidate for rtPA. Some stroke specialists recommend more aggressive blood pressure control in acute intracranial hemorrhage, but this patient has an ischemic (not hemorrhagic) stroke. Mannitol is of minimal benefit in cerebral edema associated with acute stroke.

Q9 (pretest): A 55-year-old diabetic woman suddenly develops weakness of the left side of her face as well as of her right arm and leg. She also has diplopia on left lateral gaze. Where is the responsible lesion?

A. Right cerebral hemisphere
B. Left cerebral hemisphere
C. Right side of the brainstem
D. Left side of the brainstem
E. Right median longitudinal fasciculus

Explanation: This patient has weakness of the left face and the contralateral (right) arm and leg, commonly called a crossed hemiplegia. Such crossed syndromes are characteristic of brainstem lesions. In this case, the lesion is an infarct localized to the left inferior pons caused by occlusion of a branch of the basilar artery. The infarct has damaged the left sixth and seventh cranial nerves or nuclei in the left pons with resultant diplopia on left lateral gaze and left facial weakness. Also damaged is the left descending corticospinal tract, proximal to its decussation in the medulla; this damage causes weakness in the right arm and leg. This classic presentation is called the Millard-mGubler syndrome. Hemispheric lesions cause motor and sensory loss all on the same side (contralateral to the lesion). A lesion in the median longitudinal fasciculus causes third and sixth cranial nerve dysfunction but not motor deficit of the face or body.

Answers: Q7: C | Q8: C | Q9: D

Ischemic stroke

For Questions 10 & 11 match the clinical description with the most likely mechanism of disease

Q10 (pretest): A 73-year-old woman presents with sudden-onset right-sided weakness. She has a 18-year history of type 2 diabetes mellitus which has been treated with metformin 1000 mg bid; a recent hemoglobin A1C level was 7.8. She also has hypertension and osteoarthritis. On physical examination, she is alert and oriented. BP is 172/88 and she is afebrile. Speech and mentation are normal. She has a right facial droop with sparing of the forehead. Right arm and right leg strength are 3/5; the right Babinski response is equivocal while the left is clearly downgoing. Sensory examination (including tests for stereognosis and graphesthesia) is normal bilaterally.

Q11 (pretest): A 52-year-old Hispanic man presents with left-sided weakness and difficulty with speech. He takes no medications but has noticed mild exertional dyspnea for the past 2 to 3 months. His neurological symptoms came on suddenly and without warning, like a "bolt out of the blue." He denies previous weakness or visual loss. On examination BP is 136/74 and pulse is irregular at 92/min. Cardiac examination shows an irregular rhythm and a soft diastolic rumble at the apex. He has moderate right facial weakness and pronator drift of the right hand and arm. Strength of the right leg and the left side of his body are normal. Heat-cold discrimination and light touch to microfilament testing are diminished in the right face and arm. The patient's speech is halting and nonfluent. He is unable to name simple objects such as "watch" and "pencil."

A. Large-vessel stroke due to cardiogenic embolism
B. Large-vessel stroke due to atherosclerotic middle cerebral artery (MCA) occlusion
C. CNS vasculitis due to giant cell arteritis
D. Small vessel (lacunar) stroke
E. Stroke due to carotid artery dissection
F. Hemorrhagic stroke due to uncontrolled hypertension

Explanation: Sudden onset of focal neurological deficit strongly suggests stroke. The time course and anatomic extent of involvement are important clues to the pathogenesis of the stroke, which can provide important therapeutic information. A focused history and physical examination (especially neurological examination) is the most important first step. Emergent CT scanning without IV contrast will reveal a hemorrhagic process but will initially be normal in cases of cerebral ischemia. The patient in question 373 has a lacunar (small-vessel) stroke in the internal capsule on the left. Lacunar strokes are due to occlusion of the small penetrating vessels that supply blood to subcortical white matter and brainstem; the size of the infarct will be less than 1 cm. Since the descending motor and ascending sensory fibers in the internal capsule are separate, the deficit is usually confined to one or the other. "Pure motor stroke" is the commonest lacunar syndrome. Pure sensory stroke, clumsy hand-dysarthria syndrome, and various well-localized brainstem defects are frequently seen. Cortical deficits (aphasia, seizure, cortical blindness) should not occur. Diabetes and hypertension are the usual underlying substrates for lacunar stroke. The patient in question 374 has evidence of large vessel occlusion of the left middle cerebral artery. The middle cerebral artery supplies both the motor and sensory strips of the cortex; since Broca's area is just in front of the motor cortex, an expressive aphasia is common with dominant hemisphere MCA stroke. The paramedian cortex (which controls the lower extremity) is supplied by the anterior cerebral artery; so the leg and foot are often spared in an MCA stroke. Equal involvement of face, arm, and leg suggests internal carotid occlusion (lacunar pure motor stroke also affects all three areas). Although CT or MR angiography would be necessary to distinguish embolic occlusion from atherothrombotic disease, this patient's irregular heart rhythm and murmur of mitral stenosis suggest atrial fibrillation, the commonest cause of cardiogenic embolism. Patients with stroke due to cardiogenic embolism require long-term anticoagulation; atherothrombotic and lacunar strokes are usually treated with antiplatelet drugs. Giant cell (temporal) arteritis can cause headache, fever, weight loss, and sudden visual loss due to ophthalmic artery occlusion but does not cause intracranial occlusion or stroke. Carotid artery dissection can cause stroke due to distal embolization from the intimal flap but would be associated with neck pain (usually severe); Doppler ultrasound will often show the intimal flap. Severe headache and progressive neurological deficit usually accompany hemorrhagic stroke. Hypertension is usually marked and subcortical structures (ie, thalamus, basal ganglia, cerebellum, pons) are most often affected. Obtundation suggests mass effect with brainstem compression; uncomplicated ischemic cortical strokes do not cause alterations of level of consciousness such as drowsiness or coma.

Answers: Q10: D | Q11: A

Ischemic stroke

Q12 (500Best): A 78 year old right-handed male collapses and is brought into accident and emergency. He seems to follow clear one-step commands but he gets very frustrated as he cannot answer questions. He is unable to lift his right hand or leg. He has an irregularly irregular pulse and his blood pressure is 149/87. He takes only aspirin and frusemide. What is the most likely diagnosis?

A. Left cortical infarct
B. Right internal capsule infarct
C. Left cortical haemorrhage
D. Left internal capsule haemorrhage
E. Brainstem haemorrhage

Explanation: This male has most likely suffered a left cortical infarct (A), probably as a result of an embolus secondary to atrial fibrillation. Treatment with warfarin would have reduced his annual risk of stroke from roughly 5 to 1 per cent. It is a left-sided infarct because of the contralateral (right) hemiparesis and dysphasia (involvement of the dominant cortex). It is not a capsular (B and D) or brainstem (E) event as the patient has an expressive dysphasia which implies involvement of Brocca's area which is cortical. It is more likely to be ischaemic than haemorrhagic (C). Roughly 80 per cent of strokes are infarcts, 20 per cent haemorrhagic and in this case there is a plausible embolic explanation coupled with only mild hypertension. Haemorrhagic strokes tend to occur in younger patients with severe hypertension and a family history (pointing to an anatomical anomaly). However, they cannot be differentiated clinically and a CT is required to confirm the stroke subtype.

Q13 (500Best): A 49-year-old man complains of sudden onset, painless unilateral visual loss lasting about a minute. He describes 'a black curtain coming down'. His blood pressure is 158/90, heart rate 73 bpm. There is an audible bruit on auscultation of his neck. His past medical history is insignificant other than deep vein thrombosis of his right leg ten years ago. The most likely diagnosis is:

A. Retinal vein thrombosis
B. Retinal artery occlusion
C. Amaurosis fugax
D. Optic neuritis
E. Acute angle glaucoma

Explanation: This man gives a classical description of amaurosis fugax (C), painless, unilateral visual loss of short duration described as 'a black curtain descending', caused by retinal artery emboli, with a likely cardiac source as a consequence of atrial fibrillation. Retinal artery (B) and vein (A) occlusion are also painless and of sudden onset, but they typically occur in older patients and result in prolonged visual loss. Amaurosis fugax may herald retinal artery occlusion which is confirmed on ophthalmoscopy showing oedema and a cherry red macula. It is also a complication of giant cell (temporal) arteritis. Retinal haemorrhages and cotton wool spots are typically seen in retinal vein occlusion. Optic neuritis (D) is associated with MS and patients complain of painful, blurred vision. Acute angle glaucoma (E), again seen in older patients, presents with painful, blurred vision. Patients describe 'seeing haloes around things'.

Q14 (500Best): A patient is unable to move his right arm or leg. When asked to smile, the left side of his mouth droops. Where is the lesion?

A. Left motor cortex
B. Right motor cortex
C. Left brainstem
D. Right brainstem
E. Cervical spine

Explanation: It is useful to divide the body into the areas such as: face/arms/legs, left/ right, proximal/distal. This allows a rapid diagnosis of where the lesion might be. This patient shows crossed signs. The left side of the face is affected but so is the right side of his body. Therefore, if the lesion were cortical, there would have to be two lesions to explain this (A and B). As his face is involved, there has to be a lesion above the spinal cord (E). Crossed signs tend to suggest brainstem involvement (if only one lesion is responsible). In this case a left brainstem lesion (C) would affect cranial nerves exiting on that side (LMN left-sided droop) and the cortical spinal tracts as they descend which then go on to cross at the medulla (UMN right arm and leg weakness). A right brainstem (D) lesion would cause the opposite. Please note that this is a general rule of thumb and lesions do not always result in textbook deficits.

Answers: Q12: A | Q13: C | Q14: C

Ischemic stroke

Q15 (500Best): A 60-year-old man presents with visual problems and dizziness. The dizziness started suddenly, he sees the room spinning around and he has noticed he keeps bumping into things on his right. His blood pressure is 159/91, heart rate 72. On examination, there is nystagmus and dysdiadochokinesia. Where is his stroke?

A. Temporal lobe
B. Left parietal lobe
C. Right parietal lobe
D. Anterior circulation
E. Posterior circulation

Explanation: The temporal lobe (A) is involved in memory (note: bilateral lesions required for memory to be affected), Meyer's loop of the visual pathway also pass here and lesions could result in a contralateral upper quadrantanopia. The left parietal lobe (B) is involved in language; lesions here could result in aphasia. Lesions in the right parietal lobe (C) may result in neglect (visual, sensory or motor). The patient is not blind. They are physically able to see but fail to attend to the left hemifield. Strokes in the anterior circulation (D) include those to the anterior and middle cerebral arteries which supply the frontal, temporal and parietal lobes. The posterior circulation (E) supplies the brainstem, cerebellum (coordination) and occipital lobe (vision). This would be consistent with the vertigo, right hemianopia, nystagmus and ataxia that is suggested in the vignette. Dysdiadochokinesia is the cerebellar sign of difficulty performing rapidly alternating movements.

Answers: Q15: E

Hemorrhagic stroke

Q1 (MKSAP): A previously healthy 42-year-old woman is evaluated in the emergency department for the sudden onset of a severe occipital headache during defecation 8 hours ago, followed by two episodes of vomiting. The headache reached maximum intensity within seconds. She has never had a headache like this before. She reports no neck stiffness or neurologic symptoms. Her mother and two sisters have a history of migraine. On physical examination, temperature is 36.8°C (98.2°F), blood pressure is 148/88 mm Hg, pulse rate is 90/min, and respiration rate is 20/min. The patient is in significant distress as a result of the pain. There is no evidence of meningismus, papilledema, or focal neurologic signs. Which of the following is the most appropriate next step in management?

A- CT angiography of the head and neck
B- Lumbar puncture
C- Noncontrast CT of the head
D- Subcutaneous administration of sumatriptan

Explanation: This patient should undergo noncontrast CT of the head. She has experienced a thunderclap headache, which is a severe and explosive headache that is maximal in intensity at or within 60 seconds of onset. Every thunderclap headache must be immediately evaluated to detect potentially catastrophic conditions, especially subarachnoid hemorrhage. A negative CT scan of the head should be followed by a lumbar puncture to assess for blood in the cerebrospinal fluid not detected on the CT scan. If both the CT scan of the head and lumbar puncture are negative, most of the other causes of thunderclap headache, such as an unruptured cerebral aneurysm, a carotid or vertebral artery dissection, cerebral venous sinus thrombosis, and reversible cerebral vasoconstriction syndrome, can be excluded by noninvasive angiography. CT angiography of the head and neck can detect unruptured aneurysms as small as 3 mm in diameter and thus is adequate to exclude this diagnosis. Magnetic resonance angiography (MRA) would also be appropriate in this setting. Both CT angiography and MRA can be performed with a venous phase to exclude cerebral venous sinus thrombosis. Given that most causes of thunderclap headache can be excluded by such noninvasive angiography, if prior cerebrospinal fluid analysis has shown no evidence of a subarachnoid hemorrhage, conventional cerebral angiography, in which a catheter is inserted into a large artery and advanced through the carotid artery, is unnecessary. Because the patient may have intracerebral bleeding with mass effect, the performance of a lumbar puncture could result in brainstem herniation. This is why the lumbar puncture is performed only after a CT scan is performed. If the CT scan reveals intracerebral bleeding, a lumbar puncture is unnecessary.

Q2 (MKSAP): A 73-year-old retired woman is evaluated in the emergency department 6 hours after experiencing the sudden, explosive onset of a severe headache. The patient has hypertension controlled by diet and exercise. There is no relevant family history. She has no allergies and takes no over-the-counter medications. On physical examination, she is in obvious distress from the headache. Temperature is normal, blood pressure is 179/108 mm Hg, pulse rate is 119/min, and respiration rate is 14/min. There is no meningismus. Neurologic examination shows a normal level of consciousness and no focal abnormalities. Results of laboratory studies and a CT scan of the head without contrast are normal. Which of the following is the most appropriate next management step?

A- Lumbar puncture
B- MRI of the brain
C- Observation
D- Sumatriptan, orally

Explanation: This patient should have a lumbar puncture. A thunderclap headache is a severe and explosive headache that is maximal in intensity at or within 60 seconds of onset. CT scanning is the first test to be conducted in a patient with thunderclap headache in whom a subarachnoid hemorrhage is suspected; a ruptured intracranial aneurysm is the most serious cause of such headaches. The ability to detect subarachnoid hemorrhage is dependent on the amount of subarachnoid blood, the interval after symptom onset, the resolution of the scanner, and the skills of the radiologist. On the day of the hemorrhage, extravasated blood will be present in more than 95% of patients, but in the following days, this proportion falls sharply. If an initial CT scan of the head reveals nothing, a lumbar puncture should be performed next in patients with this presentation. The finding of xanthochromia or gross hemorrhage is diagnostic for subarachnoid hemorrhage. Subsequent angiography (CT or MRI) can confirm the presence of a ruptured aneurysm in patients with a positive lumbar puncture.
Early in the diagnosis of subarachnoid hemorrhage, brain MRI is no more accurate than head CT. There is nothing to be gained by performing brain MRI in this patient with negative findings on a head CT scan.

Answers: Q1: C | Q2: A

Hemorrhagic stroke

Q3 (pretest): A 35-year-old previously healthy woman suddenly develops a severe headache while lifting weights. A minute later she has transient loss of consciousness. She awakes with vomiting and a continued headache. She describes the headache as "the worst headache of my life." She appears uncomfortable and vomits during the physical examination. Blood pressure is 140/85, pulse rate is 100/min, respirations are 18/min, and temperature is 36.8°C (98.2°F). There is neck stiffness.
Physical examination, including careful cranial nerve and deep tendon reflex testing, is otherwise normal. Which of the following is the best next step in evaluation?

A- CT scan without contrast
B- CT scan with contrast
C- Cerebral angiogram
D- Holter monitor
E- Lumbar puncture

Explanation: An excruciating headache with syncope requires evaluation for subarachnoid hemorrhage (SAH). This occurs with leakage or rupture of an intracranial aneurysm, usually located at an arterial bifurcation in the anterior cerebral circulation. Rupture may occur spontaneously or at times of exercise. About 2% of persons have "berry" aneurysms. Fortunately only a small percentage of these persons ever experience rupture, which may be fatal. The headache that precedes or accompanies SAH is severe and often described as a "thunderclap" headache, meaning that it reaches its maximum intensity in seconds. Migraine may also cause severe headache, but usually reaches maximum intensity in 5 to 30 minutes. Syncope occurs in about one-half of patients with SAH and is thought to be due to accompanying cerebral artery spasm. Blood in the cerebrospinal fluid irritates the meninges and may cause neck stiffness. Suspected subarachnoid hemorrhage mandates CT scanning as the initial test. In about 90% of patients, there will be enough blood to be visualized on a noncontrast CT scan. A contrast CT scan sometimes obscures the diagnosis because, in an enhanced scan, normal arteries may be mistaken for subarachnoid blood. If the CT scan is normal, a lumbar puncture will establish the diagnosis by demonstrating blood in the cerebrospinal fluid (CSF). As opposed to CSF blood from a traumatic lumbar puncture, the CSF blood does not clear with continued collection of fluid. Cerebral angiography is necessary to assess the need for surgery and to detect other aneurysms, but it is usually delayed because angiography may precipitate spasm, especially if performed immediately after the acute rupture. Holter monitor might be helpful in unexplained syncope but would not address the severe headache. Electroencephalography is sometimes used to diagnose seizures in a patient with unwitnessed and unexplained syncope, but would not be appropriate until subarachnoid hemorrhage has been excluded.

Q4 (500Best): A 19-year-old man is admitted with a GCS of 12. He was doing push ups when he complained of a sudden-onset, severe headache and collapsed. What would you expect on his CT?

A- Convex haematoma
B- Midline shift
C- Crescent-shaped haematoma
D- Blood along the sulci and fissures
E- Intraventricular blood

Explanation: Convex (lenticular) haematomas (A) are seen in extradural haemorrhages as the blood is trapped between the dura and the skull. These most commonly occur as a result of trauma and rupture of the middle meningeal artery. Crescent-shaped haematomas (C) indicate the blood is between the dura and arachnoid. Subdural haemorrhages occur as a result of bleeding from bridging veins, more commonly seen in the elderly and alcoholics as the veins are stretched from cerebral atrophy. Blood along the sulci and fissure (D) indicates that it is located between the arachnoid and the pia. Subarachnoid haemorrhages present clinically as a thunderclap headache which may be associated with reduced GCS and seizures. All intracranial haemorrhages require discussion with a neurosurgeon in case surgical evacuation of the clot is indicated (although it often is not). Signs that point to increased severity of bleed include midline shift (B), which indicates increased intracranial pressure, and intraventricular bleeding (E).

Q5 (AMBOSS): A 52-year-old man is brought to the emergency department because of a 2-hour history of severe, sudden-onset generalized headache. He has since developed nausea and has had one episode of vomiting. The symptoms began while he was at home watching television. Six days ago, he experienced a severe headache that resolved without treatment. He has hypertension and hyperlipidemia. The patient has smoked two packs of cigarettes daily for 30 years. His current medications include lisinopril/hydrochlorothiazide and simvastatin. His temperature is 38.1°C (100.6°F), pulse is 82/min, respirations are 16/min, and blood pressure is 162/98 mm Hg. The pupils are equal, round, and reactive to light. Fundoscopic examination shows no swelling of the optic discs. Cranial nerves II–XII are intact. He has no focal motor or sensory deficits. Finger-to-nose and heel-to-shin testing are normal. A CT scan of the head shows no abnormalities. Which of the following is the most appropriate next step in management?

A- Repeat CT scan in 24 hours
B- Obtain a lumbar puncture
C- Administer 100% oxygen and intranasal sumatriptan
D- Administer intravenous sodium nitroprusside
E- Obtain an MRI scan of the head

Explanation: If CT scan is inconclusive, lumbar puncture (LP) should be performed to rule out SAH. Even though this patient has negative head imaging (~ 90% sensitive), his sudden-onset headache with associated nausea and vomiting is highly suggestive of SAH and warrants further diagnostic work-up. He has not yet developed signs of increased intracranial pressure, which would be a contraindication for LP. Expected LP findings in SAH include elevated RBCs, high protein, xanthochromia, and possibly elevated opening pressure. It is important to distinguish SAH from a traumatic spinal tap. In SAH, the amount of RBCs remains the same in a series of collection tubes, whereas in a traumatic LP the RBC count declines (until reaching zero) over successive collection tubes.

Answers: Q3: A | Q4: D | Q5: B

Hemorrhagic stroke

Q6 (AMBOSS): A 62-year-old man is brought to the emergency department 40 minutes after his wife noticed that the right side of his face was drooping during breakfast. He had difficulty putting on his shirt and shoes before coming to the hospital. He has type 2 diabetes mellitus, hypertension, and hypercholesterolemia. His medications are metformin, enalapril, and atorvastatin. He has smoked one pack of cigarettes daily for 35 years. He drinks one glass of wine daily. He is alert and oriented to time, place, and person. His temperature is 37°C (98.6°F), pulse is 99/min, and blood pressure is 170/100 mm Hg. Examination shows equal and reactive pupils. There is drooping of the right side of the face. Muscle strength is decreased in the right upper and lower extremities. Sensation is intact. Plantar reflex shows an extensor response on the right side. Speech is dysarthric. There is a bruit on the left side of the neck. Fundoscopy shows no abnormalities. A complete blood count, coagulation profile, and serum concentrations of glucose and electrolytes are within the reference ranges. Which of the following is the most appropriate next step in management?

A- CT scan of the head
B- MRI of the brain
C- Duplex ultrasonography of the neck
D- Cerebral angiography
E- Lumbar puncture

Explanation: An emergency, noncontrast CT scan of the head is indicated as a first-line imaging technique in patients with suspected stroke to rule out intracerebral hemorrhage (ICH) and should be carried out prior to further management (e.g., thrombolysis). Additionally, a CT scan may detect signs of ischemia (e.g., hypoattenuation or large clots in a blood vessel). CT scans are fast and can significantly reduce the morbidity and mortality of stroke ("time is brain"). If the scan is inconclusive but clinical suspicion for ICH is high (e.g., due to the presence of thunderclap headache, potentially indicating subarachnoid hemorrhage), a lumbar puncture may be performed to evaluate for signs of ICH (e.g., erythrocytes) in the cerebrospinal fluid. This patient has several risk factors for stroke (e.g., diabetes mellitus, hypertension, hypercholesterolemia, and smoking) and the carotid bruit suggests a thromboembolic ischemic stroke. Findings consistent with isolated upper motor neuron weakness (right-sided facial drooping, right-sided muscle weakness, right-sided positive Babinski sign) in combination with dysarthria are highly suggestive of pure motor stroke (a type of lacunar stroke) due to occlusion of the left lenticulostriate artery.

Q7 (AMBOSS): Two days after being admitted for an ischemic stroke of the left middle cerebral artery, a 74-year-old woman is evaluated for worsening confusion. She received intravenous alteplase therapy and was admitted to the intensive care unit. Twenty-four hours after being admitted, the patient started antiplatelet therapy; she was already able to speak in full sentences and had slightly improved muscle function. While being evaluated by the physical therapist this morning, the patient was confused. Her pulse is 72/min, respirations are 12/min, and blood pressure is 120/64 mm Hg. She does not respond to verbal commands but withdraws appropriately to painful stimuli. Neurologic examination shows equal and reactive pupils. Which of the following is the most likely cause of this patient's symptoms?

A- Hemorrhagic transformation
B- Cerebral vasospasm
C- Recurrent ischemic stroke
D- Uncal herniation

Explanation: Hemorrhagic transformation (HT) is a common complication of ischemic stroke and typically manifests with neurologic deterioration (e.g., new confusion, worsening neurological deficits) within 24–48 hours of the inciting ischemic event. The risk of hemorrhagic transformation is significantly increased in patients who have received thrombolytic medications (e.g., alteplase), antiplatelet therapy (e.g., aspirin, clopidogrel), and/or thrombosis prophylaxis (e.g., heparin, enoxaparin). Other risk factors for HT include hyperglycemia, hypertension, advanced age, delayed initiation of reperfusion therapy, and large infarct size. Measures that can reduce the rate of HT include neuroprotective measures (e.g., tight blood pressure and glycemic control, targeted temperature management) and careful preselection of patients eligible for thrombolytic therapy.

Answers: Q6: A | Q7: A

Hemorrhagic stroke

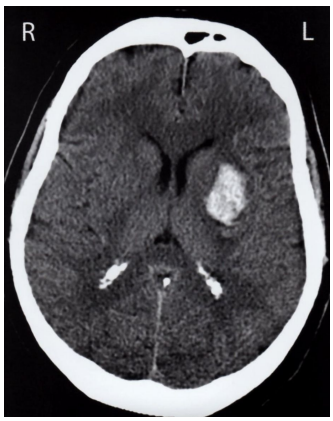
Q8 (AMBOSS): A 67-year-old woman is brought to the emergency department because of a severe headache and left-sided weakness and numbness for the past 2 hours. She has hypertension, atrial fibrillation, and type 2 diabetes mellitus. Current medications include enalapril, amlodipine, insulin, and warfarin. She is oriented to person, place, and date. Her temperature is 36.8°C (98.3°F), pulse is 90/min and irregular, and blood pressure is 165/94 mm Hg. Examination shows leftward and downward deviation of the eyes. The pupils are miotic and nonreactive. Muscle strength is 2/5 on the left side and 5/5 on the right side. Deep tendon reflexes are decreased on the left. Sensation to pinprick and light touch is decreased on the left side and normal on the right side and the face. Prothrombin time is 51 seconds (INR = 4.3). Hemorrhage into which of the following locations is the most likely cause of this patient's symptoms?

A- Cerebellum
B- Right putamen
C- Pons
D- Right thalamus
E- Right frontal lobe

Explanation: The combination of hemiparesis, hemisensory deficits, miotic and nonreactive pupils, and gaze deviation downward and toward the affected side of the body (i.e., away from the side of the brain lesion) is a phenomenon known as “wrong way eyes” and characteristically occurs in thalamic hemorrhage. In contrast, other sites of supratentorial hemorrhage typically cause a gaze deviation toward the side of the lesion (i.e., away from the affected side of the body). This patient’s left-sided weakness and sensory loss, miotic nonreactive pupils, and leftward and downward deviation of her eyes are best explained by a stroke in the right thalamus. Note that the thalamus is a relatively large region of the brain and thalamic stroke has a variety of manifestations (e.g., pure sensory stroke in lacunar syndromes). However, “wrong way eyes” is a classical finding of thalamic hemorrhage.

Q9 (AMBOSS): One day after undergoing left carotid endarterectomy, a 63-year-old man has a severe headache. He describes it as 9 out of 10 in intensity. He has nausea. He had 80% stenosis in the left carotid artery and received heparin prior to the surgery. He has a history of two transient ischemic attacks, which occurred two and four months ago, respectively. He has hypertension, type 2 diabetes mellitus, and hypercholesterolemia. He has smoked one pack of cigarettes daily for 40 years. He drinks 1–2 beers on weekends. Current medications include lisinopril, metformin, sitagliptin, and aspirin. His temperature is 37.3°C (99.1°F), pulse is 111/min, and blood pressure is 180/110 mm Hg. He is confused and oriented only to person. Examination shows pupils that react sluggishly to light. There is a right facial droop. Muscle strength is decreased in the right upper and lower extremities. Deep tendon reflexes are 3+ on the right. There is a left cervical surgical incision that shows no erythema or discharge. Cardiac examination shows no abnormalities. A complete blood count and serum concentrations of creatinine, electrolytes, and glucose are within the reference range. A CT scan of the head is shown. Which of the following is the strongest predisposing factor for this patient's condition

A- Degree of carotid stenosis
B- Aspirin therapy
C- Perioperative heparin
D- Hypertension
E- Smoking



Explanation: Arterial hypertension is the single most important predisposing factor for atraumatic intracerebral hemorrhage. Chronic hypertension results in lipohyalinosis of the arterial walls, leading to microaneurysm formation and elevated risk of rupture. Acute hypertension then leads to rupture of the weakened vessels, which likely was the mechanism of rupture in this patient. Management of intracerebral hemorrhage depends on the intracranial pressure (ICP) of the patient. If ICP is normal, blood pressure should be decreased to < 160 mm Hg through labetalol or nicardipine administration. If intracranial hypertension is suspected (as is likely in this patient, given his altered mental status and sluggishly reactive pupils), blood pressure should be lowered more cautiously, as cerebral perfusion must be maintained. Finally, if herniation is suspected (e.g., uncal herniation), emergency craniotomy is required.

Answers: Q8: D | Q9: D

Epilepsy

Q1 (500Best): A 17-year-old girl is brought into accident and emergency with generalized tonic-clonic seizure. Her mother had found her fitting in her bedroom about 20 minutes ago. The ambulance crew handover state that her sats are 96 per cent on 15 L of oxygen and they have given her two doses of rectal diazepam but she has not stopped fitting. What is the most appropriate management?

A- Lorazepam
B- Phenobarbital
C- Intubation
D- Call ITU
E- Phenytoin loading

Explanation: Status epilepticus is a serious condition of continuous seizure activity lasting more than 30 minutes. The mortality rate is one in five. This girl has been fitting for at least 20 minutes despite two doses of diazepam so must urgently be loaded with phenytoin (E) and monitored closely. ITU (D) should be alerted in case phenytoin does not stop the seizure in which case phenobarbital (B) can be considered, but the phenytoin should be given first. Ultimately, general anaesthetic and intubation (C) may be required. There is increasing evidence that lorazepam (A) is more effective than diazepam, but in this case the patient has already had two doses of benzodiazipine so the next step is phenytoin infusion.

Q2 (500Best): A 72-year-old man with known epilepsy and hypertension is admitted with pneumonia. His drug history includes aspirin, phenytoin, bendroflumethiazide and amlodipine. His heart rate is 67, blood pressure 170/93, sats 96 per cent on 2 L of oxygen. Neurological examination is normal. His doctor requests blood tests including phenytoin level. What is the correct indication for this test?

A- Routine check
B- Ensure levels are not toxic
C- Confirm patient compliance
D- Ensure therapeutic level reached
E- Reassure the patient

Explanation: Routine measurement of phenytoin levels (A) is not good practice, they should be ordered with a question in mind. They can be helpful either for adjustment of phenytoin dose or looking for toxicity or patient compliance. Phenytoin levels are useful when adjusting the dose to avoid toxicity as phenytoin has zero-order kinetics (once elimination reaches saturation rates, it cannot be cleared any faster so a small change in the dose may result in high blood levels), but there is no reason to change this patient's dose. There is no reason to suspect phenytoin toxicity either (B) as there are no signs or symptoms such as nystagmus, diplopia, dizziness, ataxia, confusion. However, his high blood pressure may be caused by non- compliance with his medication (C). Although target levels exist (D), they are imprecise and not applicable to all patients. Seizures may be well controlled with low levels, thus phenytoin should be adjusted according to the clinical picture and not levels. Levels are not helpful in reassuring the patient in this situation (E), although they often inappropriately reassure the doctor who requests them.

Q3 (500Best): A 71-year-old man with atrial fibrillation is seen in clinic following an episode of syncope. He describes getting a poor night's sleep and, as he got out of bed in the morning, feeling dizzy for a couple of seconds before the lights dimmed around him. He was woken a couple of seconds later by his wife who had witnessed the event. She says he went pale and fell to the floor and his arms and legs jerked. After waking, he was shaken but was 'back to normal' a few minutes after the event. His medication includes aspirin, atenolol and frusemide. What is the most likely diagnosis?

A- Vasovagal syncope
B- Orthostatic hypotension
C- Cardiogenic syncope
D- Transient ischaemic attack (TIA)
E- Seizure

Explanation: This man most likely experienced an episode of orthostatic or postural hypotension (B) where syncope occurs as a result of reduced cerebral perfusion as the patient moves from lying to standing. Symptoms are similar to vasovagal in that the patient may become pale and describe 'the lights or sound dimming'. Perfusion is restored after the patient collapses and unconsciousness lasts no more than seconds or a couple of minutes with full recovery. However, vasovagal epsiodes (A) can be brought on by sleep or food deprivation, hot or emotional environments, Valsalva manoeuvre (such as straining) and are not as closely related to position. Syncope while lying down is more suggestive of cardiac syncope or seizure activity. It is important to rule out cardiac causes of syncope (C) which may be heralded by chest pain or palpitations. Arrhythmias or aortic stenosis may be the underlying cause. TIAs (D) are a very rare cause of syncope. Seizures (E) may be triggered by lack of sleep. They may be heralded by an aura, typically visual or olfactory. There may be urinary incontinence, tonic-clonic movements, tongue-biting and cyanosis during the event. However, jerky movements may occur in syncope of any cause. This alone does not equate to a seizure.

Answers: Q1: E | Q2: C | Q3: B

Epilepsy

Q4 (500Best): A 23-year-old woman is seen in clinic for recurrent funny turns. She is not aware of them, but her family and friends have noticed them. They say she looks around blankly, then starts picking at her clothes and sometimes yawns, then she comes back after a minute. She can get drowsy after these episodes. What seizure type does this patient describe?

A- Absence
B- Tonic clonic
C- Simple partial
D- Complex partial
E- Generalized

Explanation: This woman has complex partial seizures (D) which start focally in the brain (classically temporal lobe) and by definition result in reduced awareness. Patients do not remember the seizure, unlike simple partial seizures (C) where consciousness is maintained. Automatisms typically characterize complex partial seizures where patients carry out repetitive and seemingly purposeless actions such as chewing, lip-smacking, picking and fumbling. Absence and tonic-clonic are types of generalized seizures (E). Absence seizures (A) typically occur in children and last seconds. Children are reported as 'staring blankly'. Seizures can be difficult to detect as they can be subtle, short-lived and the child is unaware of them. Tonic- clonic (previously called grand mal) (B) are the classic seizures where patients fall to the ground unconscious and then go through a tonic (tensing) then clonic (jerking) phase lasting seconds to minutes, typically associated with tongue-biting and incontinence and post-ictal drowsiness. Complex partial seizures may subsequently generalize but this has not been reported by this patient. Carbamazepine, lamotrigine and valproate are first-line monotherapy.

Q5 (pretest): A 68-year-old man is seen in the emergency room after an unwitnessed syncopal episode. His wife heard a strange noise and found him confused and on the floor of the living room where he had been watching television. His wife tells you that he has no ongoing medical problems, does not take any medications, and does not use alcohol or illicit drugs. On examination the patient is drowsy, has a tongue laceration, and his pants are wet with urine. Serum electrolytes (including sodium and calcium) are normal and urine drug screen is negative. Which of the following is the best next step in evaluation?

A. MRI scan of brain
B. Lumbar puncture
C. Holter monitor
D. CT scan of head
E. Echocardiography

Explanation: Though syncope is often due to a cardiovascular cause, the presence of a tongue laceration and urinary incontinence suggest syncope due to a seizure. Furthermore, patients with syncope due to cardiac causes usually recover normal mentation within a few minutes. Prolonged drowsiness is a common postictal phenomenon that can follow a generalized seizure. These findings all point to the likelihood of an unwitnessed seizure in this patient. New-onset seizure in a young person is often idiopathic or related to substance abuse (amphetamine or cocaine), but seizures that begin in older adults are worrisome for structural brain disease. The evaluation of a new seizure in an older adult includes an electroencephalogram (EEG) to confirm the diagnosis, even though the EEG will be nondiagnostic in about one-half of patients. An MRI is the best test to look for structural brain disease, such as a brain tumor, old stroke, brain abscess, or vascular malformation. Even small lesions can provide the trigger for a seizure, so the more sensitive MRI is preferred to CT scanning in this circumstance. Though often performed, routine blood tests are rarely helpful in the evaluation of seizures. Lumbar puncture is performed only if meningitis or encephalitis is suspected. Holter monitoring is used to detect rhythm disturbances that can be associated with syncope, but cardiac syncope is rarely associated with seizures. Another cause of cardiac syncope is aortic stenosis that could be detected by echocardiography, but syncope associated with aortic stenosis is almost never associated with seizures.

Answers: Q4: D | Q5: A

Epilepsy

For Questions 6 & 7 Match each scenario with the appropriate antiepileptic drug treatment

Q6 (pretest): A 67-year-old woman is admitted because of a witnessed generalized seizure associated with urinary and fecal incontinence and followed by postictal confusion. She has recently been started on hydrochlorothiazide for essential hypertension and is found to have a serum sodium level of 114 mEq/L. The neurological examination is nonfocal, and neuroimaging studies are normal. A second seizure occurs just as the infusion of 3% hypertonic saline is begun, but the patient has no further neurologic events after the serum sodium concentration is corrected. She is now ready for discharge and has a serum sodium level of 136 mEq/L. Her hypertension has responded to an angiotensin- converting enzyme inhibitor. What anti-epileptic drug regimen should be started?

Q7 (pretest): A 20-year-old woman presents to the emergency department after a witnessed seizure. She is a college student and had been awake most of the previous night studying for her final examinations. On the morning of admission she suffered a generalized seizure in the college cafeteria. There was no warning aura and no evidence of focal weakness when she was evaluated by the EMTs. The patient denies a history of seizures and denies recreational drug or alcohol use. Her father, however, has been on an unknown antiepileptic drug for many years. The patient does note that she often has muscle twitches in the morning so severe that she has dropped objects. Neurological examination and an MRI scan are both normal. Complete blood count and electrolytes are normal. What antiepileptic drug regimen should be recommended?

A. Intravenous lorazepam, 0.1 mg/kg
B. Intravenous fosphenytoin, 20 phenytoin equivalents/kg
C. Carbamazepine, 200 mg po bid
D. Phenytoin, 100 mg po tid
E. Levetiracetam 500 mg po bid
F. No treatment

Explanation: The evaluation of a first seizure should focus on (1) excluding seizure mimics such as convulsive syncope or nonconvulsive seizures (formerly termed pseudoseizures), (2) determining if the seizure is focal or primary generalized seizure, and (3) assessing the patient for secondary seizures (such as seizures caused by metabolic derangements or a structural brain abnormality such as tumor or previous stroke). Patients with a remediable cause of the seizure (as in question 382) do not need to be placed on antiepileptic drugs (AEDs). Most patients with a single unprovoked and unexplained seizure are not given AEDs, but those with high risk features for recurrence (age >65, focal findings on clinical examination, MRI, or EEG) are often offered AEDs. AEDs decrease the risk of recurrent seizures by about 50%.
The patient in question 383 has juvenile myoclonic epilepsy, an idiopathic generalized epilepsy disorder that may present in adulthood. The positive family history and the morning myoclonic jerks (sometimes dismissed by the patient "jitteriness" or ascribed to alcohol withdrawal) are characteristic. These patients require lifelong AED therapy. While most AEDs are beneficial in focal (partial) epilepsy, drugs such as phenytoin and carbamazepine may actually worsen primary generalized seizures and should not be used in this patient. Levetiracetam, lamotrigine, topira-mate, and valproic acid are better agents for primary generalized seizures. Intravenous medications such as lorazepam (the drug of first choice) and phenytoin or fosphenytoin are used in status epilepticus but would not be appropriate in either of these cases. Although status epilepticus is classically defined as continuous or repetitive seizure activity lasting longer than 30 minutes, treatment should be considered if an individual seizure lasts more than 5 minutes.

Answers: Q6: F | Q7: E

Epilepsy

Q8 (AMBOSS): A previously healthy 5-year-old boy is brought to the emergency department by his parents because of a 1-day history of high fever. His temperature prior to arrival was 40.0°C (104°F). There is no family history of serious illness. Development has been appropriate for his age. He is administered rectal acetaminophen. While in the waiting room, he becomes unresponsive and starts jerking his arms and legs back and forth. A fingerstick blood glucose concentration is 86 mg/dL. After 5 minutes, he continues having jerky movements and is unresponsive to verbal and painful stimuli. Which of the following is the most appropriate next step in management?

A. Intravenous administration of valproate
B. Intravenous fosphenytoin
C. Intravenous administration of lorazepam
D. Intravenous administration of phenobarbital
E. Rectal administration of lamotrigine

Explanation: Intravenous benzodiazepines (e.g., lorazepam, diazepam) are the first-line treatment for early status epilepticus (i.e., seizure activity lasting 5–20 minutes). Benzodiazepines increase GABAergic transmission, thereby decreasing neuronal excitability and aborting the seizure. If IV access cannot be obtained, other routes of benzodiazepine administration (e.g., intramuscular, rectal, buccal, nasal) should be used. If initial pharmacotherapy is unsuccessful, benzodiazepine administration should be repeated every 5–10 minutes. Rapidly reversible causes of seizures (e.g., hypoglycemia, hyponatremia, hypocalcemia) should be investigated and, if present, managed immediately. In persistent status epilepticus (i.e., seizure activity lasting 20–40 minutes), second-line treatment with intravenous fosphenytoin, levetiracetam, or valproate is indicated. Refractory status epilepticus (i.e., seizure activity lasting > 40 minutes) may be addressed with repetition of second-line therapy or induction of coma (e.g., with IV propofol, thiopental, midazolam, pentobarbital).

Q9 (AMBOSS): A 13-year-old boy is brought to the emergency room by his mother for a generalized tonic-clonic seizure that occurred while attending a laser light show. His mother says that he has been otherwise healthy but "he often daydreams". Over the past several months, he has reported recurrent episodes of jerky movements of his fingers and arms. These episodes usually occurred shortly after waking up in the morning. He has not lost consciousness during these episodes. Which of the following is the most appropriate treatment for this patient's condition

A. Carbamazepine
B. Diazepam
C. Valproate
D. Ethosuximide
E. Phenytoin

Explanation: Valproic acid (valproate) is the first line therapy for juvenile myoclonic epilepsy (Janz syndrome). Valproate inactivates sodium channels and inhibits GABA metabolism, increasing the concentration of GABA. Major side effects include hepatoxicity (so liver function studies must be monitored), pancreatitis, and neural tube defects (valproate is contraindicated in pregnant women).

Q10 (AMBOSS): A previously healthy 10-year-old boy is brought to the emergency department 15 minutes after he had a seizure. His mother reports that he complained of sudden nausea and seeing "shiny lights," after which the corner of his mouth and then his face began twitching. Next, he let out a loud scream, dropped to the floor unconscious, and began to jerk his arms and legs as well for about 2 minutes. On the way to the hospital, the boy regained consciousness, but was confused and could not speak clearly for about 5 minutes. He had a fever and sore throat one week ago which improved after treatment with acetaminophen. He appears lethargic and cannot recall what happened during the episode. His vital signs are within normal limits. He is oriented to time, place, and person. Deep tendon reflexes are 2+ bilaterally. There is muscular pain at attempts to elicit deep tendon reflexes. Physical and neurologic examinations show no other abnormalities. Which of the following is the most likely diagnosis?

A. Focal to bilateral tonic-clonic seizure
B. Focal seizure with dyscognitive features
C. Generalized myoclonic seizure
D. Generalized tonic-clonic seizure
E. Convulsive syncope

Explanation: ValA focal to bilateral tonic-clonic seizure (formerly called partial seizure with secondary generalization) is a seizure that begins in a limited area of one hemisphere of the brain and progresses to involve both hemispheres. Often, these seizures begin with an aura that may include feelings of nausea or seeing shiny lights. This patient's initial facial twitching and muscle contractions are characteristic of a focal seizure (repetitive movements on one side). The bilateral tonic-clonic portion of the seizure then manifests with loss of consciousness and rhythmic jerking of the extremities. After tonic-clonic seizures, consciousness usually returns slowly and a postictal phase (in this case, lethargy and confusion) begins. This patient's muscle pain on examination is likely due to the tonic muscle contractions during his seizure.

Answers: Q8: C | Q9 C | Q9 A

Dementia

Q1 (500Best): A 69-year-old man is taken to his GP by his concerned wife. She complains that he has not been himself for the last year. He has slowly become withdrawn and stopped working on his hobbies. Now she is concerned that he often forgets to brush his teeth. She has noticed he sometimes struggles to find the right word and this has gradually become more noticeable over the last couple of months. She presented today because she was surprised to come home to find him naked and urinating in the living room last week. He has a history of hypertension and is an ex-smoker. The most likely diagnosis is:

A- Depression
B- Frontotemporal dementia
C- Alzheimer's disease
D- Vascular dementia
E-Lewy Body disease

Explanation: The patient has developed a change in their behaviour. They are initially negative symptoms: withdrawal and disinterest in hobbies (as opposed to positive symptoms such as hallucinations). This would be compatible with depression (A) were it not for the development of word finding difficulties and disinhibition. These localize the problem to the temporal and frontal lobes, respectively (B). Although he is hypertensive, the progression has been gradual as opposed to the classically step-wise progression of vascular dementia (D), often these patients have had vascular events. There are no extra-pyramidal (parkinsonian) features to suggest Lewy Body disease (E). Alzheimer's disease (C) tends to affect memory and language before personality. There may be a family history, especially in someone this age, but becomes increasingly common with age. It is important to note that dementias are definitively diagnosed on biopsy/ autopsy, but this is rarely done. Differentiating between the dementias on clinical grounds can be difficult. Brain imaging may help visualizing subcortical infarcts and cortical atrophy.

Q2 (MKSAP): An 80-year old woman living in a nursing home with history of dementia is admitted to the hospital with pneumonia. In the emergency department, a peripheral intravenous line was inserted, appropriate antibiotics were initiated, she was given oxygen by nasal cannula, and a urinary catheter was placed. On physical examination, temperature is 38.3°C (101.0°F), blood pressure is 140/88 mm Hg, pulse rate is 100/min, and respiration rate is 16/min. Pulmonary auscultation reveals left lower lobe crackles. Cardiac examination is normal. Moderate cognitive impairment is noted but no inattention or focal neurologic deficits. She is provided access to her glasses and hearing aid, and a large clock and night light are in place in her room. Which of the following additional steps should be taken to prevent delirium in this patient?

A- Administer benzodiazepine, as needed
B- Administer diphenhydramine for sleep
C- Administer haloperidol twice daily
D- Check vital signs every 4 hours through the night
E- Remove her urinary catheter

Explanation: Elderly patients with a history of dementia are at very high risk for developing delirium during a hospitalization. Delirium is an acute state of confusion that may manifest as a reduced level of consciousness, cognitive abnormalities, perceptual disturbances, or emotional disturbances. Prevention involves addressing medical and environmental issues. Urinary catheters are associated with increased risk of delirium. In the absence of a medical indication for a catheter (e.g., relieve urinary retention, monitor fluid status in acutely ill patients when this directly impacts medical treatment, manage patients with stage 3 or 4 pressure ulcers on the buttocks), it should be removed.
Benzodiazepines and diphenhydramine have sedating effects but can cause delirium in the elderly. They should generally be avoided, unless a specific indication is presented, such as benzodiazepines for alcohol withdrawal or diphenhydramine for an allergic reaction. Alternative nonpharmacologic methods for relaxation include music, massage, and meditation.
In appropriate selected patients with severe delirium, low-dose haloperidol may lessen the severity and duration of delirium, but it is not indicated for the prevention of delirium. The use of antipsychotic medications in elderly patients with dementia is associated with an increased risk of death, primarily due to infection, such as pneumonia. A normal sleep-wake cycle should be maintained as much as possible, minimizing interruptions or unnecessary testing during the night, and keeping a light on and increasing stimulation during the day.

Answers: Q1: B | Q2: E

Dementia

Q3 (MKSAP): A 79-year-old woman was hospitalized 4 days ago after sustaining a right hip fracture in a fall. She underwent surgical repair with right hip replacement 3 days ago and did not fully awake from general anesthesia until 12 hours after extubation. As her alertness has increased, she has become increasingly agitated. The patient has a 4-year history of Alzheimer dementia. She has no other pertinent personal or family medical history. Current medications are donepezil, memantine, and low-molecular-weight heparin. On physical examination today, temperature is 37.2°C (99.0°F), blood pressure is 100/68 mm Hg, pulse rate is 100/min and regular, and respiration rate is 18/min. The patient can move all four limbs with guarding of the right lower limb. She is inattentive and disoriented to time and place and exhibits combativeness alternating with hypersomnolence. The remainder of the neurologic examination is unremarkable, without evidence of focal findings or meningismus. Which of the following is the most likely diagnosis?

A- Acute stroke
B- Acute worsening of Alzheimer dementia
C- Meningitis
D- Postoperative delirium

Explanation: The most likely diagnosis is postoperative delirium. Patients with delirium have acute, fluctuating mental status changes, with difficulty in focusing or maintaining attention and disorganized thinking. Based on psychomotor activity, there are four types of delirium: 1) hypoactive, 2) hyperactive, 3) mixed delirium with hypo- and hyperactivity, and 4) delirium without changes in psychomotor activity. Delirium in elderly patients with chronic dementia usually results from an acute medical problem. In addition, patients with chronic dementia from almost any cause are at greater risk for delirium after surgery with general anesthesia. This patient with a hip fracture who underwent right hip surgery with general anesthesia and did not recover from the anesthesia until 12 hours after extubation most likely has postoperative delirium. Such delirium is highly predictable and often easily managed by identification and correction of any underlying disorders and the removal or reduction of contributing factors. The possibility of acute stroke must be considered in a patient with a change in mental status. However, this patient has no clinical evidence of such an event, which makes this diagnosis extremely unlikely. Surgery does not exacerbate Alzheimer dementia (or dementia of any other cause) but rather produces a superimposed delirium. Finally, dementia does not acutely worsen over several hours; the decline is steadily progressive. This patient has had dementia for 4 years that has abruptly gotten worse after surgery. Although not impossible, meningitis is highly unlikely in this setting, especially given the absence of any supporting physical examination findings, including meningeal irritation.

Q4 (MKSAP): A 75-year-old woman is evaluated in the emergency department after she was witnessed driving erratically on a city street. Initially, the patient was unable to answer any questions and had difficulty with her speech. Twenty minutes later, her speech was fluid, and, although she did not have any recollection of the past few hours' events, she was able to provide some details of her life, including her husband's name. When her husband arrived, the patient was able to recognize him, but 10 minutes later she did not recognize him. No evidence of hallucinations or delusions exists. The husband reports that the patient has had a gradual and progressive cognitive impairment over the previous 5 years for which she takes donepezil. She often awakens at night and roams about the house. She has chronic problems with her memory and managing activities of daily living. Which of the following is the most likely diagnosis?

A- Delirium
B- Delirium superimposed on dementia
C- Dementia
D- Psychosis

Explanation: This patient has delirium superimposed on dementia. Delirium is an altered level of alertness, often in connection with globally impaired cognition. It is typically characterized by abrupt onset and may be associated with rapid fluctuations of alertness, attention, memory, and psychomotor activity (for example, lethargy or agitation). Dementia is an acquired and persistent impairment of intellectual ability that compromises at least three areas of mental functioning: language, memory, visuospatial skills, emotion or personality, or cognition. Dementia typically has an insidious onset and is usually stable from day to day. Over the protracted course of dementia, many patients may experience an acute delirium, with confused and slurred speech, somnolence, agitation, tremulousness, unsteadiness, falls, and worsened incontinence. Often, the delirium is from a superimposed illness (most commonly, a urinary tract infection or pneumonia), a medication error, an injury, or some other cause that must be sought and managed. Psychosis encompasses delusions, hallucinations, disorganized speech, and disorganized or catatonic behavior. Impaired cognition, including decrements in short-term memory and attention, is also characteristic. This patient's sudden decline in the setting of dementia and absence of hallucinations and delusions is more likely to represent an acute delirium rather than an acute psychosis.

Answers: Q3: D | Q4: B

Dementia

Q5 (MKSAP): A 73-year-old man is evaluated for confusion that began 2 weeks ago. He wanders aimlessly in the house, sometimes not recognizing his wife and mistaking the newspaper for his hat. He has visual hallucinations and believes he sees mice in the refrigerator. His medical history includes type 2 diabetes mellitus with painful peripheral neuropathy, coronary artery disease, depression, and heart failure. Medications are glyburide, nortriptyline, digoxin, lorazepam, metoprolol, lisinopril, aspirin, and pravastatin. He does not remember how long he has been taking these medications and if there have been any recent dosage changes. The patient drinks alcohol only occasionally, usually wine with a weekend meal. On physical examination, the patient has asterixis. Vital signs are normal; oxygen saturation is normal with the patient breathing ambient air. He is inattentive and not oriented to time or place. His score on the Mini-Mental State Examination is 13/30 (28/30 6 months ago). Results of laboratory studies, including electrolyte levels and liver chemistry and renal function studies, are normal. An MRI of the brain is normal.

A- Alcohol hallucinosis
B- Alzheimer dementia
C- Depression
D- Toxic encephalopathy (delirium)

Explanation: The most likely diagnosis is toxic encephalopathy presenting as delirium. Delirium is an acute state of confusion that may manifest as a reduced level of consciousness, cognitive abnormalities, perceptual disturbances, or emotional disturbances. The presence of asterixis suggests a toxic/metabolic cause of this patient's symptoms. The patient is taking several medications that might impair cognition. A prime suspect is nortriptyline; this drug has anticholinergic properties and is likely to cause impairment in patients with latent cholinergic deficiency (the elderly or patients with mild cognitive impairment, early dementia, or Parkinson disease). Digoxin and the sedative-hypnotic lorazepam may also contribute to cognitive impairment. Symptoms of alcohol withdrawal most typically occur after cessation of prolonged, sustained alcohol intake. However, most people drink in an episodic fashion, as illustrated by this patient, and this pattern of drinking is not associated with sustained high blood alcohol levels that are requisite for withdrawal symptoms on abrupt cessation. Alcoholic hallucinosis develops 12 to 24 hours after the last drink and resolve within 24 to 48 hours, a symptomatic period much shorter than that experienced by this patient. Hallucinations are usually visual and are not associated with clouding of the sensorium and are not associated with asterixis. In patients with early Alzheimer dementia, delirium is produced more readily by anticholinergic medications. Alzheimer dementia cannot be ruled out in this patient, but establishing the diagnosis would require removal of the causative agent and re-evaluation after recovery. However, asterixis, a sign of metabolic encephalopathy, would be unusual in this setting and points strongly to a metabolic encephalopathy and not dementia. Depression may cause chronic cognitive impairment (pseudodementia) and difficulty concentrating, but not asterixis and an altered level of consciousness.

Q6 (MKSAP): An 84-year-old man is evaluated for the gradual onset of progressive memory loss over the past 2 years. In the past 4 months, he has twice been unable to find his way home after going to the local supermarket. His wife has assumed responsibility for the household finances after the patient overdrew their checking account for the third time. His mother had onset of Alzheimer dementia at age 79 years and died at age 86 years. His only medication is a daily multivitamin. On physical examination, vital signs are normal. His level of alertness, speech, and gait are normal. His score on the Folstein Mini-Mental State Examination is 24/30, including 0/3 on the recall portion, which corresponds with a diagnosis of mild dementia. Results of laboratory studies, including a complete blood count, serum vitamin B12 measurement, thyroid function tests, and a basic metabolic panel, are normal. An unenhanced MRI of the brain shows no abnormalities. Which of the following is the most appropriate treatment at this time?

A- Donepezil
B- Ginkgo biloba
C- Quetiapine
D- Sertraline

Explanation: This patient should receive donepezil. This patient has Alzheimer dementia and is at a mild stage of impairment. The most appropriate medication with which to begin treatment is an acetylcholinesterase inhibitor of which there are currently three: donepezil, rivastigmine, and galantamine. In patients with mild, moderate, or severe Alzheimer dementia the use of acetylcholinesterase inhibitors are associated with a small but statistically significant improvement in performance of instrumental and functional activities of daily living and caregiver stress and may be associated with improved cognitive function compared with patients treated with placebo. Treatment effects are small and not always apparent in practice. Cholinesterase inhibitors are generally safe but have significantly more side effects than placebo, including diarrhea, nausea, vomiting, and symptomatic bradycardia. The gastrointestinal side effects are usually transient and mild. Ginkgo biloba, although safe, has inconsistent and unconvincing evidence of benefit in the treatment of Alzheimer dementia. Also, there is no regulation regarding the contents of herbal extracts, which allows for variability in dose strength and quality.

Answers: Q5: D | Q6: A

Dementia

Q7 (MKSAP): A 68-year-old man is evaluated for memory difficulty that, according to his wife, began insidiously 3 or 4 years earlier. He has difficulty remembering recent events. For example, he forgets appointments and recent conversations and forgot that a close relative had recently died. He is no longer able to manage his own checkbook or operate his car without getting lost. Medical history is otherwise unremarkable. Physical examination findings, including vital signs, are normal. Mental status examination shows prominent memory loss and difficulty drawing a complex figure. Laboratory studies show that a complete blood count and routine chemistries are normal. An MRI of the brain shows only mild cerebral atrophy.

A- Alzheimer dementia
B- Creutzfeldt-Jakob disease
C- Dementia with Lewy bodies
D- Frontotemporal dementia

Explanation: The most likely diagnosis is Alzheimer dementia. Dementia is a clinical syndrome in which multiple cognitive domains—including memory, language, spatial skills, judgment, and problem solving—are impaired to a disabling degree. Some dementing illnesses can also affect noncognitive neurologic functions, such as gait. Diseases that cause dementia often produce characteristic patterns of cognitive (and sometimes noncognitive) impairment that can aid diagnosis. Alzheimer dementia is characterized by prominent memory loss, anomia, constructional apraxia, anosognosia (impaired recognition of illness), and variable degrees of personality change. Creutzfeldt-Jakob disease (CJD) is the most common of the human prion diseases, with an annual incidence of less than 1 in 1,000,000 persons. The main clinical features of CJD are dementia that progresses over months (rather than years, as in this case) and startle myoclonus, although the latter may not be present early in the illness. Other prominent features include visual or cerebellar disturbance, pyramidal/extrapyramidal dysfunction, and akinetic mutism. Dementia with Lewy bodies is accompanied by parkinsonism, visual hallucinations, and fluctuating symptoms, none of which this patient has. The characteristic cognitive profile of dementia in patients with dementia with Lewy bodies includes impaired learning and attention, psychomotor slowing, constructional apraxia, and more profound visuospatial impairment but less memory impairment than in similarly staged patients with Alzheimer dementia. Frontotemporal dementia is a progressive neuropsychiatric condition. Patients initially have behavioral and personality changes that range from apathy to social disinhibition. They fail to change their clothes, brush their teeth, pursue their former interests, or initiate many of their previous activities that constituted a normal day. They may fixate, in a seemingly idiosyncratic fashion, on a particular activity, such as going to the bathroom, sorting through a wallet, hoarding magazines, or watching television. Some patients have greater disinhibition and emotional lability (crying or laughing inappropriately).

For Questions 8-10 select the most likely diagnosis, For each of the clinical descriptions

Q8 (pretest): An 80-year-old woman has developed gradually progressive memory loss; she is aware of her deficit, which is frustrating to her. Over the past month or two, she has had difficulty controlling her voiding to the point that she is now using adult diapers. Her gait has become unsteady, with a shuffling lurching quality and frequent falls. MRI shows dilated ventricles bilaterally, normal sulci, and no mass lesion.

Q9 (pretest): A 70-year-old man with history of hypertension and diabetes presents with a stepwise loss of intellectual function. Earlier episodes have been associated with unilateral weakness and difficulty swallowing. A unilateral Babinski sign is found on neurological examination.

Q10 (pretest): A 52-year-old man presents with emotional lability, weight loss, and hallucinations. Over several months he has developed a rapidly progressive dementia associated with quick jerks of his arms and legs that are precipitated by movement. An electroencephalogram is abnormal with diffuse slowing and periodic sharp waves. Cerebrospinal fluid analysis shows normal cell count, glucose, and protein.

A. Senile dementia of Alzheimer type
B. Creutzfeldt-Jacob disease
C. Vascular (multi-infarct) dementia
D. Vitamin B12 deficiency
E. Tertiary syphilis
F. Dementia with Lewy bodies
G. Normal-pressure hydrocephalus

Answers: Q7: A | Q8: G | Q9: C | Q10: B

Dementia

Explanation: The development of a dementing illness is a catastrophe for patient and family alike. Once it is clear that multiple domains (not just memory) are affected, and that the defect is interfering with daily function, evaluation for “treatable” causes of dementia is indicated. The triad of cognitive decline, recent onset of urinary incontinence, and apraxia of gait should suggest normal pressure hydrocephalus (NPH). The gait disturbance resembles parkinsonism, but leg function will usually be near-normal in the supine position. CNS imaging (either CT or MRI) will reveal enlargement of ventricles out of proportion to cortical atrophy. Some of these patients will improve or stabilize in response to CSF shunting (usually into the peritoneum); deciding which patients are candidates for a shunt procedure is complicated and is often guided by the patient’s response to a temporary CSF drainage procedure. The 70-year-old with hypertension and previous focal deficits is most likely to have vascular dementia. This is associated with progressive stepwise deterioration, usually the result of recurrent bilateral cortical or sub-cortical (lacunar) infarcts. Focal findings, including hemiparesis, extensor plantar responses, and pseudobulbar palsy, are common. Creutzfeldt-Jacob disease is a rare form of dementia that is distinguished from other dementias by early personality change, a rapidly progressive course, the presence of myoclonus (90% of patients), and distinctive EEG abnormalities (periodic sharp waves). In these patients the cerebrospinal fluid cell count, glucose, and protein levels are normal, but the 14-3-3 protein is often present. The causative agent is a prion or transmissible protein. The disease usually occurs sporadically though familial cases have been reported. Transmission has also occurred by consumption of contaminated beef as well as by transplantation of affected tissue such as dura mater, cornea, or pituitary gland. Creutzfeldt-Jacob disease is rapidly fatal with death occurring in most cases within a year of symptom onset. Alzheimer disease (AD), the commonest cause of dementia, is steadily and inexorably progressive. Insight and judgment often deteriorate along with memory; so the patient is not usually aware of the deficit. Dementia with Lewy bodies (DLB) causes dementia with bradykinesia, visual hallucinations, and sensitivity to the side effects of anticholinergic medications. Although both AD and DLB may show temporary response to cholinergic medications, the underlying process is inexorably progressive. Vitamin B12 deficiency can cause a dementing illness, often but not always in association with a macrocytic anemia and decrease in proprioception and vibratory sensation. Tertiary syphilis can cause parenchymal destruction and dementia, but is much less common than in previous eras. Often there is a compatible history or evidence of tabes dorsalis (severe neuropathy). Evaluation for treatable causes of dementia include medication history, thyroid studies, B12 (or methylmalonic acid) level, chemistry panel (to exclude renal failure or electrolyte imbalance), and CNS imaging. Further evaluations such as RPR, lumbar puncture, or specialized testing, are reserved for those with atypical feature (such as rapid progression) or a compatible history..

Answers: Q7: A | Q8: G | Q9: C | Q10: B

Peripheral neuropathies

Q1 (500Best): A 31-year-old woman presents to accident and emergency with progressive difficulty walking associated with lower back pain. A few days ago she was tripping over things, now she has difficulty climbing stairs. She describes tingling and numbness in both hands which moved up to her elbows, she is unable to write. On examination, cranial nerves are intact but there is absent sensation to vibration and pin prick in her upper limbs to the elbow and lower limbs to the hip. Power is 3/5 in the ankles and 4−/5 at the hip with absent reflexes and mute plantars. Her blood pressure is 124/85, pulse 68 and sats 98 per cent on air. She has a past medical history of type I diabetes and recently recovered from an episode of food poisoning a month or two ago. What is the diagnosis?

A- MS
B- Guillain–Barré syndrome (GBS)
C- Myasthenia gravis
D- Diabetic neuropathy
E- Infective neuropathy

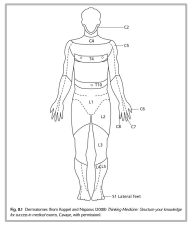
Explanation: This woman presents with an ascending polyneuropathy. Her symptoms start distally and progress proximally, giving a glove and stocking distribution. Both sensory and motor neurones are involved. This is consistent with Guillain–Barré (B), an inflammatory disorder of the peripheral nerves often preceded by an infection such as campylobacter gastreoenteritis. Multiple sclerosis (A) is an inflammatory disorder of the central nervous system resulting in upper motor neurone signs – this patient's reflexes are absent. Myasthenia gravis (C) is a disorder of the neuromuscular junction and although it results in lower motor neurone signs, there is no sensory involvement and the weakness is greater in proximal muscles and commonly involves the cranial nerves resulting in droopy eyelids, difficulty speaking and swallowing. A key feature is fatigability as the stores of acetylcholine are used up. Although this woman is diabetic and has a polyneuropathy, her symptoms progress too quickly. Diabetic neuropathy (D) takes time to develop and, although there are different types, most commonly results in a distal sensory neuropathy of the feet. Vibration and pain are most affected which is why they may have a stomping gait and develop ulcers. Infective neuropathies (E) include Lyme disease from ticks and leprosy which is uncommon in developed countries and she has no history of travel.

Q2 (500Best): You are asked to perform a lower limb peripheral neurological examination on a 45-year-old diabetic male. The patient has normal tone, 5/5 power, normal plantars and proprioception. However, you notice that the patient does not respond to any sensory stimulus on the medial side of the right lower leg. Which dermatome is affected?

A- L1
B- L2
C- L3
D- L4
E- L5

Explanation: The dermatomes of the lower leg are important to know when performing
a lower limb neurological examination. If the upper leg is divided into three equal thirds from the greater trochanter to the knee L1 (A), L2 (B) and L3 (C) correspond to these dermatome areas. If the lower leg is split into two sides down to the ankle, the medial side of the leg corresponds to dermatome L4 (D), while L5 (E) extends from the lateral side of the lower leg down to the dorsum of the great toe.

Q3 (500Best): On examination, a patient has 5/5 power in his upper limbs, 0/5 power in his lower limbs. Further examination reveals a sensory level at the umbilicus. Cranial nerves are intact. Where is the lesion?



A- C4
B- T4
C- T10
D- L1
E- L3

Explanation: Like the previous question, this patient is paraplegic. The lesion can be in the thoracic or lumbar cord. A sensory level helps further identify the location of the lesion. Dermatomes overlap and are not always consistent. You do not need to be able to delineate every dermatome but it is useful to have a general idea of certain levels such as: C4 shoulders (A), T4 nipples (B), T10 umbilicus (C), L1 pockets (D), L3 knee (E) (see Figure 8.1).

Answers: Q1: B | Q2: D | Q3: C

Peripheral neuropathies

Q4 (MKSAP): A 53-year-old woman is evaluated in the office for a 1-week history of paresthesias that began symmetrically in the feet and progressed to involve the distal legs and, more recently, the hands. She is unsteady when walking, has lower limb weakness, and has difficulty going upstairs. The patient has no history of pain or bowel or bladder impairment. Personal and family medical history is noncontributory, and she takes no medications. On physical examination, vital signs are normal. Weakness of distal lower extremity muscles is noted, with stocking-glove sensory loss and areflexia. Deep tendon reflexes are absent. Plantar responses are normal, and gait is unsteady. No sensory level is present across the thorax. Mental status, language, and cranial nerve function are normal. Complete blood count results, erythrocyte sedimentation rate, serum creatinine and creatine kinase levels, and liver chemistry test results are normal. A chest radiograph shows no abnormalities. Which of the following is the most likely diagnosis?

A- Amyotrophic lateral sclerosis
B- Diabetic neuropathy
C- Guillain-Barre syndrome
D- Myelopathy

Explanation: This patient has a rapidly progressive disorder affecting the peripheral nervous system, most compatible with a clinical diagnosis of Guillain-Barre syndrome. Patients with Guillain-Barre syndrome typically develop paresthesias distally in the lower extremities that are followed by limb weakness and gait unsteadiness. In addition to sensory loss and limb weakness, deep tendon reflexes are characteristically absent or markedly reduced. The diagnosis is confirmed by electromyography, which usually shows a demyelinating polyradiculoneuropathy. Cerebrospinal fluid (CSF) analysis characteristically shows albuminocytologic dissociation, whereby the spinal fluid cell count is normal but the spinal fluid protein level is elevated. CSF analysis may also yield normal results early in the course of the disease. However, a normal CSF cell count is useful in excluding other infectious conditions, such as polyradiculoneuropathies associated with HIV and cytomegalovirus infection, infection due to West Nile virus, and carcinomatous or lymphomatous nerve root infiltration. By definition, symptoms in patients with Guillain-Barre syndrome peak within 4 weeks of onset. Intravenous immune globulin and plasma exchange are equally efficacious in the treatment of Guillain-Barre syndrome. Amyotrophic lateral sclerosis (ALS) is a degenerative disease of the anterior horn cells of the spinal cord and presents with both upper and lower motor neuron signs, including hyperreflexia, spasticity, and an extensor plantar response (upper motor neuron signs) and weakness, muscle atrophy, and fasciculations (lower motor neuron signs). The patient's findings are not compatible with ALS. Diabetes mellitus most commonly causes a slowly progressive, distal, symmetric sensorimotor polyneuropathy. Autonomic dysfunction frequently is associated with diabetic neuropathy and is characterized by symptoms of impotence, orthostatic hypotension, and gastroparesis. The symptoms of a distal symmetric sensorimotor neuropathy may be the first clinical manifestation, but the rapidly progressive course of this patient's neuropathy rules out diabetic neuropathy. A spinal cord lesion (myelopathy) would be an unlikely cause of the symptoms noted on clinical examination. The absence of bowel or bladder impairment, the lack of a sensory level across the thorax, and the upper and lower limb areflexia argue against a central nervous system disorder affecting the spinal cord.

Q5 (MKSAP): A 35-year-old woman is evaluated in the office for a 5-month history of right-hand numbness and tingling. She says that these symptoms involve the entire hand, seem to be worse when she drives or holds a book or newspaper, and have been awakening her at night. She reports no history of neck pain or hand weakness. Personal and family medical histories are noncontributory, and she takes no medication. General physical examination reveals no abnormalities. Neurologic examination shows normal strength but sensory loss in the first three digits and the radial half of the fourth digit in the right hand. Which of the following is the most likely diagnosis?

A- Carpal tunnel syndrome
B- de Quervain tenosynovitis
C- Ganglion cysts
D- Ulnar nerve compression (Guyon tunnel syndrome)

Explanation: This patient most likely has carpal tunnel syndrome. Carpal tunnel syndrome refers to median nerve compression at the wrist in the carpal tunnel. Symptoms include aching wrist pain with sparing of the palm, numbness and tingling in the median nerve sensory distribution of the fingers, and weakness of the thenar muscles. The paresthesias are often worse at night or when holding a book or steering a car. de Quervain tenosynovitis is an exercise-related injury associated with knitting and sports involving extensive wrist action. Tenderness may be elicited in the anatomic snuffbox (the extensor pollicis brevis and abductor pollicis longus tendons). Pain elicited by flexing the thumb into the palm, closing the fingers over the thumb, and then bending the wrist in the ulnar direction (Finkelstein test) is confirmatory. Ganglion cysts are synovia-filled cysts arising from joints or tendon sheaths that typically appear on the dorsal hand or ventral wrist. They can cause pain and compress other structures. The absence of cystic structures on the dorsal and ventral wrist and the distribution of the patient's pain eliminate this diagnosis. Ulnar nerve compression at the wrist is also called Guyon tunnel syndrome, because the entrapment occurs where the ulnar nerve transverses the Guyon tunnel between the pisiform and hamate bones on the anterolateral side of the wrist, and cyclist's palsy, because the compression of the ulnar nerve often occurs as the hand rests on the handlebars. However, the ulnar nerve can be compressed by muscles, tumors (lipomas), scar tissue, synovial cysts, or any other internal structure that passes close to the tunnel. The presentation is similar to that of carpal tunnel syndrome, but with symptoms and signs on the ulnar distribution of the hand.

Answers: Q4: C | Q5: A

Peripheral neuropathies

Q6 (pretest): A 50-year-old man complains of slowly progressive weakness over several months. Walking has become more difficult, as has using his hands. There are no sensory, bowel, or bladder complaints; he denies problems with thinking, speech, or vision. Examination shows distal muscle weakness with muscle wasting and fasciculations. There are also upper motor neuron signs, including extensor plantar reflexes and hyperreflexia in wasted muscle groups. The remainder of the neurological examination is unremarkable. Which of the following tests is most likely to be abnormal in this patient?

A. Cerebrospinal fluid white blood cell count
B. Sensory nerve conduction studies
C. CT scan of the brain
D. Electromyography
E. Thyroid studies and vitamin B12 level

Explanation: This patient's findings are worrisome for the progressive motor neuron disease amyotrophic lateral sclerosis (ALS). Amyotrophic lateral sclerosis affects both upper and lower motor neurons but spares the sensory and autonomic systems. Upper motor neuron signs include an extensor plantar response and an increased tendon reflex in a weakened muscle. Lower motor neuron signs include focal weakness, focal wasting, and fasciculations. Muscular dystrophy, polymyositis, and the neuromuscular junction disorder myasthenia gravis cause (usually proximal) muscle weakness but not the atrophy, fasciculations, and upper motor neuron signs seen in this patient. EMG in the patient with ALS shows widespread denervation and fibrillation potentials with preserved nerve conduction velocities. Sensory testing is normal. There is no inflammatory reaction in the CSF. CT or MRI of the brain and cervical spine may be necessary to rule out a mass in themregion of the foramen magnum or cervical cord compression as can be seen in cervical spine stenosis, but would not be the first test chosen. Thyroid studies and vitamin B12 levels may be useful in peripheral neuropathy but not in motor neuron disease.

Q7 (500Best): A 66-year-old woman complains of stiffness and weakness climbing stairs. She has a history of hypertension and diet-controlled type 2 diabetes. On examination, there is mild upper arm weakness, hip flexion is 4−/5 bilaterally, with bilateral wasting and flickers of fasciculations in the right quadriceps. Knee extension is 4/5. Dorsiflexion and plantar flexion are strong. Brisk knee and ankle reflexes are elicited, as well as a positive Hoffman's and Babinski's sign. Sensory examination and cranial nerves are normal. Her BM is 8.9, her pulse is regular and her blood pressure is 178/97. What is the most likely diagnosis?

A- Myasthenia gravis
B- Diabetic neuropathy
C- Myositis
D- Motor neurone disease
E-Multiple sclerosis (MS)

Explanation: This woman presents with upper (brisk reflexes, upgoing plantar) and lower (fasciculations) motor neurone signs. Motor neurone disease (MND) (D) presents with mixed upper and lower motor neurone signs and importantly no sensory involvement. In this case, there is involvement of two regions (arms and legs). Bulbar signs, such as tongue wasting and fasciculation, often help make the diagnosis. Myositis (C) affects the muscle, resulting in tenderness, wasting and fasciculation but no upper motor neurone (UMN) signs. Although the patient is diabetic, neuropathies (B) result in lower motor neurone (LMN) signs only. These may be motor and/or sensory. Typically, diabetes results in a peripheral neuropathy, most commonly sensory. The proximal distribution of weakness would be in keeping with myasthenia (A), but not the UMN signs. There is no mention of fatigability, which is a key feature. MS (E) in this age group is less common and an inflammatory disorder of the central nervous system would not result in LMN signs.

Answers: Q6: D | Q7:D

Peripheral neuropathies

Q8 (500Best): A 45-year-old man presents with a 5-day history of progressive tingling and numbness of his hands and feet. He insists that he has never had this problem before and that he was perfectly fine a week ago. Over the last 2 days he has had some difficulty walking but mostly he complains about difficulty rolling up cigarettes. On examination, there is mild symmetrical distal weakness, mild gait ataxia and dysdiadochokinesia. He smokes 30 cigarettes a day and drinks 1–2 bottles of wine. He has a family history of hypertension and his 63-year-old mother has type 2 diabetes, whom over the last year has complained of numbness and burning in her feet. He self-discharges. A week later, his symptoms have peaked. He displays moderate distal weakness and numbness to his knees, after which he turns a corner and his symptoms start to slowly resolve. What is the diagnosis?

A. Miller Fisher syndrome
B. Alcoholic neuropathy
C. Chronic idiopathic demyelinating polyneuropathy
D. Charcot Marie Tooth disease
E. GBS

Explanation: The key is in the timing: speed of onset, time to peak and resolution. This is why it is crucial to elicit a clear timeline of events. This man has an acute peripheral polyneuropathy (both sensory and motor involvement). The timing is consistent with GBS (E). Chronic idiopathic demyelinating polyneuropathy (CIDP) (C) has a slower rate of onset and resolution over months, if indeed it does resolve, and patients are also prone to relapse. Miller Fisher syndrome (A) is a variant of GBS, exhibiting the classic triad of ophthalmoplegia, ataxia and areflexia. Although the patient shows ataxia, this could be related to his alcohol intake. The neuropathy in Miller Fisher syndrome classically starts proximally with involvement of the eyes and face (the opposite of GBS where deficits starts distally and work their way proximally). Alcoholic neuropathy tends to progress slowly and may resolve slowly on abstinence. In rarer cases, it is acute. Charcot Marie Tooth disease is a hereditary neuropathy, symptoms start much earlier in life and it is often accompanied by a family history. His mother may have diabetic neuropathy which has developed later in life. This man's lifestyle needs to be addressed in terms of advice, as well as support, to prevent future disease.

Answers: Q8: E

Parkinson's disease

Q1 (500Best): A left-handed 79-year-old man presents with a troublesome resting tremor of his left hand. The tremor is evident in his writing. He has also noticed his writing is smaller than it used to be. He complains he has difficulty turning in bed to get comfortable and his wife complains that he sometimes kicks her in the middle of the night. When he gets out of bed in the morning he feels a little woozy, but this resolves after a while. On examination, he blinks about three times a minute and his face does not show much emotion. Glabelar tap is positive. He has a slow, shuffling gait. He has difficulty stopping, starting and turning. He holds his feet slightly apart to steady himself. When you pull him backwards, he is unable to right himself and stumbles back. Which of the signs and symptoms is not commonly associated with parkinsonism?

A- Postural instability
B- Rapid eye movement (REM) sleep disturbance
C- Hypomimia
D- Broad-based gait
E- Autonomic instability

Explanation: This man presents with many symptoms of parkinsonism. However, the parkinsonian gait is typically narrow-based, not broad (D). Parkinson's is a disease of dopaminergic neurone loss in the nigrostriatal pathways and results in the triad of bradykinesia, rigidity and tremor. A fourth sign to look out for is postural instability (A). This can be elicited by asking the patient to steady himself and pulling him backwards. During REM sleep (B), the brain is active but muscles are paralysed (thus associated with dreaming). In Parkinson's disease (PD), muscles may be active allowing patients to act out their dreams, resulting in kicking, yelling, etc. Hypomimia (C) is the technical term for mask-like facies or reduced facial expression. Symptoms of autonomic dysfunction (E) are common and include constipation, postural hypotension and sexual dysfunction. Very prominent autonomic symptoms may suggest Shy–Drager's, a type of multiple system atrophy (which in turn is one of the Parkinson's plus syndromes).

Q2 (pretest): A 47-year-old dentist consults you because of tremor, which is interfering with his work. The tremor has come on gradually over the past several years and seems more prominent after the ingestion of caffeine; he notices that, in the evening after work, an alcoholic beverage will decrease the tremor. No one in his family has a similar tremor. He is otherwise healthy and takes no medications. On examination his vital signs are normal. Except for the tremor, his neurological examination is normal; in particular there is no focal weakness, rigidity, or bradykinesia. When he holds out his arms and extends his fingers, you detect a rapid fine tremor of both hands; the tremor goes away when he rests his arms at his side. What is the best next step in the management of this patient?

A- MRI scan to visualize the basal ganglia
B- Electromyogram and nerve conduction studies to more fully characterize the tremor
C- Therapeutic trial of propranolol
D- Therapeutic trial of primidone
E- Neurology referral to rule out motor neuron disease

Explanation: This patient's action tremor (ie, brought out by sustained motor activity) and otherwise normal neurological examination are diagnostic of essential tremor. Fifty percent of patients will have a positive family history (benign familial tremor). The tremor is termed "benign" to separate it from Parkinson disease and other progressive neurological diseases and because it does not affect other areas of function; however, about 15% of patients (especially those in professions that require fine motor control) will be functionally impaired. An identical rapid fine action tremor can be seen in normal persons after strenuous motor activity or with anxiety. Hyperthyroidism, caffeine overuse, alcohol withdrawal, and use of sympathomimetic drugs (such as cocaine and amphetamines) can cause an identical tremor and can exacerbate the tremor in familial cases. Neurological imaging is normal in patients with essential tremor. The EMG is nonspecific. This patient has no features (eg, weakness, fasciculations) to suggest motor neuron disease. Patients with essential tremor are managed with medications, especially beta-blockers, to decrease the severity of the tremor. Most neurologists feel that nonselective beta-blockers (blocking both beta-1 and beta-2 receptors) are most effective. They can be used on an "as needed" basis (ie, before performance of fine tasks) if the patient is not troubled by the tremor at other times. Primidone is also effective but is associated with more side effects, especially at higher doses.

Answers: Q1: D | Q2: C

Parkinson's disease

Q3 (pretest): A 74-year-woman consults you because of tremor and difficulty completing her daily tasks on time. She has hypertension and takes hydrochlorothiazide 25 mg every morning. She does not smoke and uses alcohol infrequently. On examination, her BP is 126/84; her vital signs are otherwise unremarkable. Eye movements are normal as are her reflexes and motor strength. She moves slowly; her timed up-and-go (TUG) test takes 24 seconds (normal 10 seconds). She has a slow resting tremor with a frequency of about 3 per second; the tremor is more prominent on the right than the left. The tremor decreases with intentional movement. Her handwriting has deteriorated and is small and crabbed. Which therapy is most likely to improve her functional disabilities?

A. Switching her antihypertensive to propranolol 20 mg po bid
B. Benztropine mesylate 0.5 mg po tid
C. Lorazepam 0.5 mg po tid
D. Ropinirole beginning at a dose of 0.25 mg tid
E. Carbidopa/levodopa beginning at a dose of one-half of a 25 mg/100 mg tablet tid

Explanation: Parkinson disease (PD) is marked by depletion of dopamine-rich cells in the substantia nigra. The resulting decrease in striatal dopamine is the basis for the classic symptoms of rigidity, bradykinesia, tremor, and postural instability. Many experts consider bradykinesia to be the fundamental feature of PD. Although tremor is often the first manifestation, about 20% of patients do not have a tremor. When present, the tremor occurs at rest, is slower than most other tremors, and decreases with intentional activity (so that a watch repairman with PD is often able to function normally). The most effective treatment for PD is levodopa. Levodopa is converted to dopamine in the substantia nigra and then transported to the striatum, where it stimulates dopamine receptors. This is the basis for the drug's clinical effect on PD. Levodopa is usually administered with carbidopa (a dopa decarboxylase inhibitor) in one pill. Carbidopa prevents levodopa's metabolism in the peripheral circulation and central nervous system, and thus allows it to be given at a lower dose less likely to cause nausea and vomiting. The major problems with levodopa have been (1) limb and facial dyskinesias, (2) motor fluctuations ("off-on" effects), and (3) the fact that levodopa treats PD only symptomatically while neuronal loss in the substantia nigra continues despite drug treatment. Direct dopamine agonists (such as ropinirole or pramipexole), although less potent than dopa-mine itself, are often used as the first drug in younger patients. Side effects (in particular, motor fluctuations) are often less troublesome. Anticholinergic agents, such as benztropine mesylate, work by restoring the balance between striatal dopamine and acetylcholine; they are particularly effective in decreasing the degree of tremor. In the elderly, however, they often cause CNS side effects (especially confusion) and would not be a good choice in this elderly woman. Propranolol would help essential tremor but has no benefit in Parkinson disease. Chronic benzodiazepine use should be avoided because of the risk of habituation as well as confusion and falls in the elderly. Benzodiazepines do not improve the symptoms of PD.

Q4 (AMBOSS): A 59-year-old woman comes to the physician because of progressively worsening coordination and involuntary movements in her left hand for the past 6 months. Her husband also reports that she has been withdrawn and apathetic during this period. She is oriented to time, place, and person. Examination shows a bimanual, rhythmic, low-frequency tremor that is more prominent in the left hand. There is normal range of motion in the arms and legs; active movements are very slow. Muscle strength is normal, and there is increased resistance to passive flexion and extension in the limbs. She walks with a shuffling gait and takes small steps. Which of the following is the most likely underlying cause of this patient's symptoms?

A. Accumulation of neurotoxic metabolites secondary to hepatocyte damage
B. Copper accumulation due to mutations in hepatocyte copper-transporting ATPase
C. Neuronal degeneration due to α-synuclein protein misfolding
D. Cerebellar ischemia due to chronic hypertension
E. Proliferation of beta-adrenergic receptors from excessive circulating T4

Explanation: Neuronal degeneration due to α-synuclein protein misfolding is the hallmark of Parkinson disease (PD), a disease characterized by the presence of eosinophilic inclusions known as Lewy bodies in the soma of neurons. Lewy bodies are aggregates of misfolded α-synuclein and other proteins and are also seen in patients with Lewy body dementia and multiple system atrophy (MSA). Although α-synuclein dysfunction is a key process in PD pathogenesis, the factors instigating neurodegeneration and the selective loss of dopaminergic neurons are multifaceted and still under investigation.

Answers: Q3: E | Q4: C

Parkinson's disease

Q5 (AMBOSS): A 67-year-old man comes to the physician because of a worsening tremor that began 1 year ago. The tremor affects his left hand and improves when he uses his hand to complete a task. He also reports feeling stiffer throughout the day, and he has fallen twice in the past year. He has not noticed any changes in his cognition or mood. He has not had difficulty sleeping, but his wife says that he would kick and punch while dreaming for almost a decade. He drinks two cans of beer daily. He takes no medications. He appears well nourished. Vital signs are within normal limits. The patient maintains a blank stare throughout the visit. Further evaluation is most likely to show which of the following?

A. Reduced amplitude on foot tapping
B. Startle myoclonus
C. Choreiform movements
D. No abnormalities
E. Horizontal gaze nystagmus

Explanation: Slowed and reduced amplitude of repetitive movements (e.g., foot tapping, opening and closing the hand, or tapping thumb and index fingers) is a sign of bradykinesia, which is a hallmark feature of PD. In PD, degeneration of dopaminergic neurons in the substantia nigra leads to a deficiency of dopamine in the striatum. Dopamine deficiency in the striatum in turn causes decreased excitatory signaling to the motor cortex, which results in bradykinesia and akinesia. Other common features of PD include shuffling gait, postural instability, and micrographia. The diagnosis of PD is clinical; additional tests, including imaging, are not routinely required but should be considered in patients with atypical presentation or to rule out other disorders. To establish the diagnosis of PD, patients must present with bradykinesia in addition to tremor or rigidity.

Q6 (AMBOSS): A 47-year-old man is brought to the office by his wife because of unusual behavior for the past 2 weeks. His wife reports that the patient spent a large sum of money at the local casino and bought a new car without consulting her. He has been sleeping poorly. She says, "This is very unusual for him. Yesterday, he also tried to flirt with my best friend at a birthday party while I was just 5 feet away." He has hypertension, restless legs syndrome, and allergic rhinitis. His medications are propranolol, ropinirole, and budesonide nasal spray. He does not smoke cigarettes, drink alcohol, or use illicit drugs. He is 178 cm (5 ft 10 in) tall and weighs 82 kg (180 lb); BMI is 26 kg/m2. Vital signs are within normal limits. When asked about his mood, the patient replies, "I feel fine. I just had to buy that car; she's such a beauty. I want to get out of here to take her for a ride!" The remainder of the examination shows no abnormalities. Which of the following is the most appropriate next step in management?

A. Involuntary hospitalization
B. Prescribe risperidone
C. Reduce ropinirole dose
D. Refer for cognitive behavioral therapy

Explanation: Dopamine agonists (DAs) such as ropinirole may lead to impulse control disorders (ICDs), irrespective of the underlying disease. Patients taking DAs should be aware of this adverse effect and regularly monitored, because ICDs may have debilitating effects on their work and social functioning. If the patient shows signs of ICDs, the dose should be slowly tapered or discontinued until symptoms resolve. Abrupt discontinuation of DAs can lead to dopamine agonist withdrawal syndrome. Although most patients with ICDs due to DA therapy respond well to discontinuation of the medication, ICDs may persist in some patients. Other adverse effects of DAs include restlessness, nausea, orthostatic hypotension, drowsiness, hallucinations, and psychosis.

Q7 (AMBOSS): A 76-year-old woman with Parkinson disease comes to the physician with worsening tremor, shuffling gait, and unsteadiness despite taking levodopa/carbidopa combination medication three times daily. Neurologic examination shows a high frequency resting tremor of both hands, markedly slowed finger- and toe-tapping, and rigidity of the upper extremities. Her gait is slow, with shortened stride length. Selegiline is added to her medication regimen. Which of the following is the most likely mechanism of action of this drug?

A. Blockade of central methylation of levodopa
B. Increased release of dopamine from central neurons
C. Inhibition of central oxidative deamination of dopamine
D. Decreased peripheral conversion of levodopa to dopamine
E. Decreased peripheral conversion of levodopa to dopamine

Explanation: Selegiline is a monoamine oxidase B inhibitor (MAO-B inhibitor) that can be used as an alternative to levodopa or dopamine agonists to treat Parkinson disease with mild symptoms or as an adjunct to treat advanced motor symptoms, as seen in this patient. MAO-B inhibitors reduce the metabolism of dopamine, which increases its concentration in the basal ganglia. It has also been proposed that selegiline has a secondary neuroprotective mechanism, blocking free radicals formed during dopamine metabolism. Common adverse effects of selegiline include nausea, headache, and insomnia. In older patients, selegiline can also precipitate confusion.

Answers: Q5: A | Q6: C | Q7: C

Parkinson's disease

Q8 (AMBOSS): A 55-year-old woman comes to the physician because of a 6-month history of worsening involuntary movement of the left hand. She also reports that it takes her longer than usual to get up from a chair. Her symptoms are worse when she feels stressed at work. She has no history of serious illness and takes no medications. Neurological examination shows difficulty initiating movement and a tremor in the left hand at rest. The tremor decreases when the patient is asked to draw a circle. Which of the following is the most appropriate pharmacotherapy?

A. Clonazepam
B. Methimazole
C. Propranolol
D. Trihexyphenidyl
E. Pramipexole

Explanation: A non-ergot dopamine agonist such as pramipexole or ropinirole is the typical first-line treatment for Parkinson disease in young patients (< 65 years) without cognitive impairment. If symptoms are severe, combination treatment of levodopa with carbidopa and/or a COMT inhibitor (e.g, entacapone) can be initiated. Levodopa is more effective than dopamine agonists. However, levodopa therapy is usually reserved for elderly patients or patients with cognitive impairment.

Q9 (AMBOSS): A 58-year-old woman comes to the physician because of a 6-month history of difficulty walking, clumsiness of her arms and legs, and slurred speech. Physical examination shows masked facies and a slow, shuffling gait. When her ankles are passively flexed, there is involuntary, jerky resistance. Treatment is initiated with a combination of levodopa and carbidopa. The addition of carbidopa is most likely to decrease the risk of which of the following potential adverse drug effects?

A. Resting tremor
B. Orthostatic hypotension
C. Visual hallucinations
D. Dyskinesia

Explanation: Following administration, L-DOPA is absorbed into the systemic circulation where it is partially converted to dopamine by the enzyme DOPA decarboxylase. The remaining L-DOPA is then transported across the blood-brain barrier and enters the central nervous system to produce the desired effects. Carbidopa reduces the peripheral (systemic) conversion of L-DOPA to dopamine, thereby mitigating the peripheral sides effects, including orthostatic hypotension, nausea, and vomiting. Although the combination of carbidopa-levodopa significantly improves drug compliance, many patients still experience some degree of these side effects.

Q10 (AMBOSS): A 72-year-old woman comes to the physician because she is seeing things that she knows are not there. Sometimes she sees a dog in her kitchen and at other times she sees a stranger in her garden, both of which no one else can see. She also reports a lack of motivation to do daily tasks for the past week. Three years ago, she was diagnosed with Parkinson disease and was started on levodopa and carbidopa. Her younger brother has schizophrenia. The patient also takes levothyroxine for hypothyroidism. She used to drink a bottle of wine every day, but she stopped drinking alcohol 2 months ago. Neurologic examination shows a mild resting tremor of the hands and bradykinesia. Her thought process is organized and logical. Which of the following is the most likely underlying cause of this patient's symptoms?

A. Adverse effect of medication
B. Alcohol withdrawal
C. Schizophrenia
D. Major depressive disorder
E. Poorly controlled hypothyroidism

Explanation: Levodopa (L-DOPA), a dopamine precursor, is the most effective medication for controlling the motor symptoms of Parkinson disease. Primary effects of L-DOPA are achieved by stimulating D2-receptors in the substantia nigra and striatum. However, overstimulation of D2-receptors by levodopa may also induce psychosis and hallucinations (usually visual). The risk for developing psychiatric symptoms increases with age, other psychiatric conditions, long duration of levodopa treatment, and high doses. Since this patient has been taking levodopa for 3 years and is elderly, her symptoms are most likely the result of levodopa therapy. Other adverse effects of L-DOPA therapy include dizziness, somnolence or insomnia, anxiety, and aggressive behavior.

Answers: Q8: E | Q9: B | Q10: A

Myopathies

Q1 (pretest): A 45-year-old woman presents to her physician with a 6-week history of gradually increasing limb weakness. She first noticed difficulty climbing stairs, then problems rising from a chair, and, finally, lifting her arms above shoulder level. Aside from some difficulty swallowing, she has no ocular, bulbar, or sphincter problems and no sensory complaints. Family history is negative for neurological disease. Examination reveals significant proximal limb and neck muscle weakness with minimal atrophy, normal sensory findings, and normal deep tendon reflexes. Affected muscles are slightly tender; there is no skin rash. What is the likely pathogenesis of her condition?

A. B- and T-cell mediated attack against muscle autoantigens
B. Anterior horn cell degeneration in the spinal cord
C. Antibodies to the acetylcholine receptor at the neuromuscular junction
D. Vasculitis with focal nerve and muscle necrosis
E. Abnormal trinucleotide repeat in the DMPK gene

Explanation: Polymyositis is an acquired myopathy characterized by subacute symmetrical weakness of proximal limb and trunk muscles that progresses over several weeks or months. When a characteristic skin rash occurs, the disease is known as dermatomyositis. Both of these disorders are felt to have an autoimmune pathogenesis. Autoantibodies (including antinuclear antibodies and antibodies to the Jo-1 antigen) are common, and up to 50% of cases will have additional features of connective tissue diseases (rheumatoid arthritis, lupus erythematosus, scleroderma, Sjögren syndrome). Laboratory findings in polymyositis include an elevated serum CK level, an EMG showing myopathic potentials with fibrillations, and a muscle biopsy showing necrotic muscle fibers and inflammatory infiltrates. Anterior horn cell degeneration of unknown cause characterizes amyotrophic lateral sclerosis (ALS), but evidence of denervation (such as muscle fasciculations) and upper motor neuron involvement (hyperreflexia) would be expected. ALS is often asymmetric at onset. Antibodies to the acetylcholine receptor (AchR) are seen in myasthenia gravis (MG), but other autoantibodies and in particular evidence of direct immunological attack against muscle fibers do not occur. The weakness in MG is episodic and usually brought on by prolonged exertion; ptosis and diplopia (indicative of involvement of the bulbar musculature) are common in MG but rare in polymyositis. Vasculitis (for instance, polyarteritis nodosum) typically affects nerves more than muscles, usually causing an asymmetric mononeuritis multiplex. Systemic involvement such as fever, necrotic skin lesions, and renal involvement would be expected in a vasculitic process. Muscular dystrophies cause insidious onset of muscle weakness and wasting and will present with pure motor weakness without other evidence of neurological abnormality. Muscular dystrophy, however, would be uncommon at this age in a patient with negative family history. Myotonic muscular dystrophy is associated with abnormal CTG trinucleotide repeat in the DMPK gene and can present in adulthood, but would be expected to cause myotonia, cardiac dysfunction, and distal muscle weakness.

Q2 (AMBOSS)): A 42-year-old woman comes to the physician because of a 2-month history of progressive muscular weakness. She has had difficulty climbing stairs, getting up from chairs, and brushing her hair. Her vital signs are within normal limits. Muscle strength is 2/5 with flexion of the hips and 3/5 with abduction of the shoulders. She is unable to stand up from her chair without the use of her arms for support. Laboratory studies show elevations in leukocyte count, erythrocyte sedimentation rate, and creatine kinase concentration. Histological evaluation of a biopsy specimen of the deltoid muscle is most likely to show which of the following?

A. Sarcolemmal MHC-I overexpression with CD8+ lymphocytic infiltration
B. Relative atrophy of type II muscle fibers with hypertrophy of type I muscle fiber
C. Perimysial inflammation with perivascular CD4+ T lymphocytic infiltration
D. Muscle fiber necrosis with rare inflammatory cells

Explanation: This patient has symmetric proximal muscle weakness with elevated muscle and inflammatory markers without dermatologic findings, which is consistent with a diagnosis of polymyositis. Histological examination of skeletal muscles affected by polymyositis typically shows endomysial infiltration of CD8+ lymphocytic T cells and macrophages, with areas of muscle necrosis and regeneration of muscle fibers. In addition, overexpression of MHC-I on the sarcolemma is an immunohistochemical finding that is classic for polymyositis. Muscle atrophy is not a prominent feature of this disorder, in contrast to dermatomyositis. Polymyositis is associated with positive ANA (30–60% of cases), positive anti-Jo-1 (25% of cases), and malignancy (15–20% of cases).

Answers: Q1: A | Q2: A

Myopathies

Q3 (AMBOSS): A 43-year-old woman comes to the physician because of a 2-month history of progressive muscle pain and stiffness that worsens with exercise. She also has difficulty climbing stairs, getting out of chairs, and putting things on shelves or in cupboards. She has had constipation, occasional headaches, and a 9-kg (20-lb) weight gain during the past year. She has hypertension controlled with atenolol and amlodipine. She has used calamine lotion for the past 6 months for dry skin. Her pulse is 80/min and her blood pressure is 138/76 mm Hg. Physical examination shows weakness of the proximal muscle groups. She has delayed tendon reflex relaxation, with a mounding of the muscle surface occurring just before relaxation. Creatine kinase level is 3120 U/L. Which of the following is the most appropriate next step in diagnosis?

A. Needle electromyography
B. Genetic testing
C. Serum TSH levels
D. Temporal artery biopsy

Explanation: This patient presents with typical symptoms of hypothyroidism, including weight gain, dry skin, constipation, and myopathy. In individuals with hypothyroidism, a shortage of thyroid hormone leads to decreased metabolic function, characterized by decreased protein turnover and carbohydrate metabolism, which often manifests in the muscles. Muscle pain on exertion is a typical feature of impaired carbohydrate metabolism. Hypothyroid myopathy typically manifests with slowed contraction and delayed relaxation of muscles. The best initial step here is to determine TSH levels and FT4 levels to confirm the diagnosis.
Other typical features of hypothyroidism include fatigue, cold intolerance, hair loss, abnormal menstrual cycle, impaired cognition, and depression. Normal TSH levels very likely rule out hypothyroidism and hyperthyroidism and are therefore the definitive screening test for both conditions.

Q4 (AMBOSS): A 16-year-old boy is brought to the physician by his parents because of a 9-month history of progressive difficulty walking and muscle weakness that has forced him to quit his cycling team. During this period, he also has had problems climbing stairs and standing up from a seated position. He is at the 65th percentile for height and weight. Examination shows enlargement of both calf muscles and a waddling gait. Serum creatine kinase concentration is 540 U/L. Genetic analysis shows an in-frame deletion in the dystrophin gene. This patient is at greatest risk of dying from which of the following conditions?

A. Coronary artery disease
B. Respiratory failure
C. Congestive heart failure
D. Pulmonary embolism

Explanation:This adolescent patient's features (difficulty standing from a seated position, waddling gait, bilateral calf pseudohypertrophy) in conjunction with markedly elevated creatine kinase (CK) and an in-frame deletion of the dystrophin gene, are suggestive of Becker muscular dystrophy (BMD). Congestive heart failure from dilated cardiomyopathy is the most common cause of death in patients with Becker muscular dystrophy (BMD). The in-frame deletion affecting the dystrophin gene causes a partially functional dystrophin protein, which leads to muscle tissue necrosis and subsequent cardiac fibrosis. Although patients with BMD generally have less severe musculoskeletal symptoms with a slower disease progression than patients with Duchenne muscular dystrophy (DMD), cardiac involvement is more common and is a considerable cause of morbidity.

Q5 (AMBOSS): A 56-year-old woman comes to the physician because of a 3-month history of progressive weakness. She has no history of serious illness and takes no medications. Her vital signs are within normal limits. Physical examination shows a violaceous rash over her eyelids. Muscle strength is 4/5 at the shoulders and hips but normal elsewhere. This patient is at greatest risk for which of the following conditions?

A. Hodgkin lymphoma
B. Ovarian adenocarcinoma
C. Oat cell lung cancer
D. Pheochromocytoma

Explanation: Patients with dermatomyositis are at increased risk of developing malignancies, particularly ovarian adenocarcinomas in the case of female patients. Other malignancies associated with inflammatory myopathies such as dermatomyositis include adenocarcinomas of the cervix, lungs, ovaries, and bladder. Diagnostic criteria for dermatomyositis include detection of anti-Mi-2 and anti-Jo-1 antibodies and parafascicular and perivascular infiltration with plasmacytoid dendritic cells and B lymphocytes on biopsy.

Answers: Q3: C | Q4: C | Q5: B

Myopathies

Q6 (AMBOSS): A 3-year-old boy is brought to the physician by his parents because of a 6-month history of worsening mobility issues. During this period, his parents noticed that he had occasional falls and increasing difficulties climbing stairs and running. The boy had a normal development up until then; he was able to walk by the age of 15 months. There is no personal or family history of serious illness. He takes no medications and immunizations are up-to-date. He is at the 10th percentile for height and 25th percentile for weight. Vital signs are within normal limits. Musculoskeletal examination shows enlarged calf muscles bilaterally. Deep tendon reflexes are 1+ on the lower extremities and 2+ on the upper extremities. He has a waddling gait and when asked to get up from the floor, he supports himself with his hands on his legs to get to an upright position. Which of the following is the most appropriate initial step in diagnosis?

A. Muscle biopsy
B. Genetic analysis
C. Serum creatine kinase concentration
D. Electromyography

Explanation: This boy presents with a waddling gait, hyporeflexia in the lower extremities, bilateral calf pseudohypertrophy, and Gower maneuver. The early onset of these symptoms suggests Duchenne muscular dystrophy (DMD). DMD is an x-linked recessive disease characterized by progressive muscle paresis and atrophy that typically starts in the pelvic girdle, as seen in this patient. Because DMD results in a deficiency of dystrophin, affected muscle cells die, leading to elevated serum levels of creatine kinase (CK). In almost all cases of DMD, serum CK levels are 20–100 times the upper limit of the reference range by the age of 2 years (i.e., even before the onset of symptoms of DMD) and then decline at the rate of approx. 25% per year due to progressive replacement of muscle tissue by fat and fibrotic tissue. If DMD is suspected, serum CK concentration should be obtained as the first step in diagnosis and genetic analysis for DMD gene mutations should then be performed to confirm the diagnosis. If the CK level is normal or only mildly increased at the time of symptom onset, DMD is unlikely and a different condition (e.g., spinal muscular atrophy) should be considered. Genetic analysis is a complex and expensive procedure and is only performed if the results of another initial step are suggestive of DMD. Genetic analysis is used to confirm the diagnosis of DMD. As DMD is characterized by a deficiency of dystrophin, muscle biopsy showing the absence of dystrophin can confirm the diagnosis. However, a muscle biopsy is an invasive procedure and is only performed if other, less invasive tests are unavailable or inconclusive.

Q7 (AMBOSS): A 47-year-old woman comes to the physician because of progressive muscle weakness for 5 months. She feels that the muscles in her shoulders and hips have been getting weaker and sometimes feel sore. She now has difficulty getting up from chairs, climbing stairs, and combing her hair. She has also noticed new difficulty with swallowing solid foods but has no trouble with liquids. She has a 5-year history of hyperlipidemia controlled with fluvastatin. Family history is remarkable for Hashimoto thyroiditis in her mother and Duchenne muscular dystrophy in her maternal uncle, who died at age 26 years. Vital signs are within normal limits. Neurologic examination shows moderate weakness in the arm abductors and hip flexors bilaterally. Deep tendon reflexes are 2+ bilaterally. Laboratory studies showed, Which of the following is most likely to confirm the diagnosis?

Hemoglobin	13.7 g/dL
Leukocyte count	11,000/mm^3
Erythrocyte sedimentation rate	33 mm/h
Serum	
Creatine kinase	212 U/L
Lactate dehydrogenase	264 U/L
AST	54 U/L
ALT	55 U/L

A. Resolution of symptoms with statin cessation
B. Perifascicular and perivascular infiltration on muscle biopsy
C. Dystrophin gene mutation on genetic analysis
D. Intrafascicular infiltration on muscle biopsy

Explanation: This patient has symmetric proximal muscle weakness with elevated muscle and inflammatory markers without dermatologic findings, which is consistent with a diagnosis of polymyositis (PM). Inflammatory cellular infiltrates of cytotoxic T cells within muscle fascicles are a characteristic finding on histological examination of muscle biopsies in patients with PM. The most common clinical feature of PM is slowly progressive, symmetric proximal muscle weakness, typically including the deltoids and the hip flexors. Dysphagia for solids may occur due to the involvement of the upper esophageal striated muscles. Laboratory findings are typically nonspecific, with mildly elevated levels of inflammatory markers (e.g., CRP, ESR) and muscle enzymes (e.g., creatine kinase, lactate dehydrogenase, AST, and ALT), as found in this patient. Other possible laboratory findings include elevations of myoglobin and autoantibodies (e.g. antinuclear antibodies, myositis-specific antibodies). Muscle biopsy is the confirmatory test of choice for inflammatory myopathies (see table “Differential diagnoses of myopathies”).
The first-line treatment for PM is systemic corticosteroids, which improve strength and muscle function. In patients who cannot tolerate steroids, other immunosuppressive agents, e.g., rituximab, are used.

Answers: Q6: C | Q7: D

Myopathies

Q8 (AMBOSS): A 3-year-old boy is brought to the physician by his parents because of clumsiness and multiple falls over the past 4 months. He started walking at the age of 18 months and could walk up steps by the time he was 27 months old but now struggles to walk at all without assistance. When standing up from a lying position, he crawls onto his knees and slowly walks himself up with his hands. There is bilateral calf enlargement. Analysis of a left calf biopsy specimen from this patient is most likely to show which of the following?

A. Proliferation of mitochondria within muscle fibers
B. Atrophic muscle fibers interspersed among hypertrophic muscle fibers
C. Perivascular inflammation with muscle fiber ischemia and atrophy
D. Degeneration of muscle fibers with fibrofatty replacement

Explanation: The presence of calf pseudohypertrophy and the Gower sign in this patient are highly suggestive of Duchenne muscular dystrophy. Degeneration of muscle fibers with fibrofatty replacement is the underlying pathology of muscular dystrophies such as Duchenne muscular dystrophy. Muscle fiber degeneration occurs due to dystrophin gene mutations, which lead to alterations of the dystrophin protein. Complete impairment of dystrophin results in disturbance of cellular signaling pathways, which promotes necrosis in these cells. Subsequently, these muscle cells are replaced with connective and fat tissue and the muscle appears larger (calf pseudohypertrophy).

Q9 (AMBOSS): A 3-year-old boy is brought to the emergency department because of nausea and vomiting for 1 day. His maternal uncle had a seizure disorder and died in childhood. He appears fatigued. Respirations are 32/min. Examination shows diffuse weakness in the extremities. Serum studies show a low pH, elevated lactate concentration, and normal blood glucose. A metabolic condition characterized by a defect in oxidative phosphorylation is suspected. Microscopic examination of a muscle biopsy specimen of this patient is most likely to show which of the following findings?

A. Muscle atrophy with perimysial inflammation
B. Intermyofibrillar accumulation of glycogen
C. Subsarcolemmal accumulation of mitochondria
D. Endomysial inflammation with T-cell infiltration

Explanation: This patient's presentation of metabolic acidosis (manifesting as tachypnea), elevated serum lactate, and diffuse muscle weakness is most likely due to lactic acidosis. Subsarcolemmal and intermyofibrillar accumulation of mitochondria in muscle fibers is a hallmark of mitochondrial diseases, which are characterized by defective oxidative phosphorylation and subsequent lack of energy. The compensatory proliferation of mitochondria presents as characteristic ragged-red fibers on Gomori trichrome stain. This patient's lactic acidosis and diffuse muscle weakness in combination with the family history of CNS disease and childhood death suggest a form of mitochondrial myopathy, most likely MELAS syndrome.

Answers: Q8: D | Q9: C

Neuromuscular junction disorders

Q1 (500Best): A 55-year-old woman complains of double vision. She finds that she is more tired than usual and has difficulty climbing stairs, especially when they are very long. She has difficulty getting items off high shelves at work and lately even brushing her hair is a problem. During the consultation, her voice fades away during conversation. Reflexes are present and equal throughout. Which sign or symptom is most indicative of myasthenia gravis?

A- Proximal weakness
B- Normal reflexes
C- Diplopia
D- Fatigability
E- Bulbar symptoms

Explanation: Disease of the muscle and neuromuscular junction can be similar. Both generally tend to affect proximal muscles (A). Cranially, this may result in ptosis and ophthalmoplegia (C) as well as bulbar symptoms (E) such as dysphagia and hypophonia. In both cases, reflexes (B) and muscle bulk tend to be preserved or, if severe and longstanding, reduced. A key clinical feature that differentiates myopathies and MG is fatigability (D). As patients with myasthenia use their muscles, they exhaust the supply of acetylcholine, resulting in increasing weakness. This can be elicited by asking the patient to repeatedly abduct and adduct one arm and compare it to the other arm that has remained at rest. Alternatively, you can ask the patient to count to 100 and their voice will fatigue, or ask them to do squats or test neck flexion.

Q2 (500Best): A 55-year-old woman complains of double vision. She finds that she is tired all the time and has difficulty climbing stairs. She has difficulty getting items off high shelves at work. Reflexes are absent but elicited after exercise. Shoulder abduction is initially 4–5 but on repeated testing is 4 +/5. What pathology is associated with this female's diagnosis?

A- Thyrotoxicosis
B- Peptic ulcer
C- Diabetes
D- Stroke
E- Lung cancer

Explanation: In contrast to MG, patients with Lambert–Eaton myasthenic syndrome (LEMS) experience increased strength upon repetition. LEMS is a rare disease caused by autoantibodies against the voltage-gated calcium channels on the presynaptic motor nerve terminal. It is a paraneoplastic disorder, most often associated with small-cell lung cancer (E), although a variety of underlying malignancies may be the culprit. LEMS may be difficult to differentiate from MG clinically, an EMG is key for diagnosis as well as testing for autoantibodies and searching for underlying malignancy. MG is associated with other autoimmune disease such as thyrotoxicosis (A), haemolytic and pernicious anaemia, connective tissue disease, as well as thymomas, which is why a thymectomy is often performed. Neither MG nor LEMS are directly associated with petic ulcer, diabetes or stroke (B, C, D).

Q3 (AMBOSS): A 51-year-old woman with hyperlipidemia comes to the physician because of weakness for one month. At the end of the day, she feels too fatigued to cook dinner or carry a laundry basket up the stairs. She also complains of double vision after she reads for long periods of time. All of her symptoms improve with rest. Her only medication is pravastatin. Physical examination shows drooping of the upper eyelids. Strength is initially 5/5 in the upper and lower extremities but decreases to 4/5 after a few minutes of sustained resistance. Sensation to light touch is intact and deep tendon reflexes are normal. Which of the following best describes the pathogenesis of this patient's condition?

A. Type II hypersensitivity reaction
B. Peripheral nerve demyelination
C. Impaired acetylcholine release
D. Adverse drug effect
E. Anterior horn cell destruction

Explanation: Type II hypersensitivity reactions are characterized by antibody-mediated cellular destruction, cellular dysfunction, and/or inflammation. In myasthenia gravis, autoantibodies bind to post-synaptic acetylcholine receptors (AChR) at the neuromuscular junction, resulting in the inhibition of these receptors and impairing the process of neuromuscular transmission. Other examples of similar type II hypersensitivity reactions involving antibody-receptor binding include Graves disease and pemphigus vulgaris.

Answers: Q1:D | Q2:E | Q3: A

Neuromuscular junction disorders

Q4 (AMBOSS): A 53-year-old man comes to the physician because of a 3-month history of cough and progressively worsening difficulty walking up the stairs in his apartment. He has noticed that it is easier for him to climb the stairs after he has exercised. He has also had a 4.6-kg (10-lb) weight loss over the past 6 months. He has smoked one pack of cigarettes daily for 35 years. Examination shows dry mucous membranes. The pupils are equal and react sluggishly to light. Muscle strength in the proximal lower extremity is initially 3/5 but increases to 5/5 after repeated muscle tapping. His Achilles reflex is 1+. Which of the following is the most likely diagnosis?

A. Amyotrophic lateral sclerosis
B. Polymyalgia rheumatica
C. Myasthenia gravis
D. Lambert-Eaton syndrome
E. Dermatomyositis

Explanation: Lambert-Eaton myasthenic syndrome (LEMS), which is associated with small-cell lung cancer in two-thirds of cases, is caused by circulating autoantibodies that block presynaptic voltage-gated calcium channels (anti-VGCC antibodies) at the neuromuscular junction. This blockage impairs acetylcholine (ACh) release, which leads to reduced or absent deep tendon reflexes and proximal muscle weakness; the latter improves during exercise as repetitive nerve stimulation increases the amount of ACh in the synaptic cleft. Patients with LEMS may also develop symptoms of autonomic dysfunction such as a dry mouth, constipation, or impotence.

Q5 (AMBOSS): A 28-year-old woman comes to the physician because of a 1-year history of progressive weakness. During this time, she has had increasing difficulty climbing the stairs to her 5th-floor apartment, worsening double vision, and fatigue. There is no personal or family history of serious illness. She works as a teacher and finds it increasingly difficult to pursue her occupation because of her symptoms. Muscle strength is 3/5 on abduction of the shoulders and flexion of the hips, and 4/5 in the remaining muscle groups of all extremities. Sensation is intact bilaterally. Deep tendon reflexes are 2+ and symmetric. On cranial nerve examination, there is drooping of the upper eyelids and she reports double vision when moving her eyes. Placement of an ice pack on her eyelids for 2 minutes improves the eyelid drooping. Her serum thyroid-stimulating hormone (TSH) concentration is 4.2 µU/mL. Results of other screening lab studies are within the reference ranges. Which of the following is the most likely diagnosis?

A. Polymyositis
B. Polymyalgia rheumatica
C. Myasthenia gravis
D. Lambert-Eaton syndrome
E. Multiple sclerosis

Explanation: Myasthenia gravis (MG) typically affects older men (40-70 years of age) and younger women (20-40 years of age) and is characterized by ptosis, diplopia, and proximal limb weakness. A positive ice pack test supports the diagnosis of MG. The presence of acetylcholine receptor antibodies in the serum and electromyography showing a decremental response following repetitive nerve stimulation confirms the diagnosis. Treatment with acetylcholinesterase inhibitors (e.g., pyridostigmine) is the standard approach in MG. Supplemental immunosuppression with glucocorticoids is added if symptoms persist despite treatment with pyridostigmine.MG is also associated with other autoimmune diseases such as Hashimoto thyroiditis, which this patient may have (indicated by increased TSH).

Q6 (AMBOSS): A 63-year-old man comes to the physician for the evaluation of difficulty walking for the last 6 months. He reports weakness in his lower legs that improves with exercise and throughout the day. Three months ago, he started adding flax seeds to his breakfast because he is frequently constipated.. Vital signs are within normal limits. Examination shows dry mucous membranes. Muscle strength in the lower extremities is decreased. Sensation to pinprick and light touch is normal. Deep tendon reflexes are 1+ bilaterally. Active muscle contraction or repeated muscle tapping increases reflex activity. Which of the following is most likely to confirm the diagnosis?

A. Demyelinating plaques on a brain MRI
B. Autoantibodies against voltage-gated calcium channels
C. Single Fiber Electromyography (SFEMG)
D. Decremental response following repetitive nerve stimulation
E. Acetylcholine Receptor (AChR) Antibodies.

Explanation: Patients with LEMS have autoantibodies against the P/Q voltage-gated calcium channels at the presynaptic motor neuron. In patients with LEMS, the levels of acetylcholine in the neuromuscular junction are decreased because the autoantibodies impair the release of acetylcholine from the presynaptic terminal of the motor endplate. This results in reduced neuromuscular transmission and muscle weakness. Repetitive nerve stimulation during exercise or during nerve conduction studies increases the amount of acetylcholine in the synaptic cleft, which improves muscle strength and the amplitude of muscle action potentials (since the postsynaptic ACh receptors remain intact). About two-thirds of all cases of LEMS are associated with an underlying malignancy, most commonly small-cell lung cancer. Given this association and the patient's 90-pack year smoking history, it is imperative that he undergoes a chest X-ray and/or CT.

Answers: Q4: D | Q5: C | Q6: B

Neuromuscular junction disorders

Q7 (AMBOSS): A 50-year-old man comes to the physician because of diffuse weakness for the past several months. A lateral x-ray of the chest that was recently obtained as part of a preemployment medical evaluation shows an anterior mediastinal mass. He has gastroesophageal reflux disease. His only medication is rabeprazole. He is 178 cm (5 ft 10 in) tall and weighs 77 kg (170 lb); BMI is 24 kg/m2. Vital signs are within normal limits. There is no cervical or axillary lymphadenopathy. Cardiopulmonary examination shows no abnormalities. The abdomen is soft and nontender; there is no splenomegaly. Further evaluation of this patient is most likely to show which of the following?

A. Fever, night sweats, and weight loss
B. Smoking history of 30 pack years
C. Elevated serum alpha-fetoprotein level
D. Acetylcholine receptor antibodies
E. Elevated TSH and a nodular anterior cervical mas

Explanation: Acetylcholine receptor antibodies are used to diagnose myasthenia gravis, a condition that is present in about 30% of patients with thymoma and manifests with fatigable weakness of skeletal muscles. Almost all patients with thymoma and myasthenia gravis are seropositive for these antibodies, which target postsynaptic nicotinic acetylcholine receptors of normal muscle cells and inhibit signal transduction at the neuromuscular junction. Thymectomy can improve muscle weakness and even cure myasthenia gravis. Patients with thymoma may be asymptomatic or present with thoracic symptoms (e.g., chest pain, cough, dyspnea, superior vena cava syndrome) or paraneoplastic syndromes (e.g., myasthenia gravis)..

Q8 (AMBOSS): A 42-year-old woman comes to the physician because of progressive weakness for the past month. She has noticed increasing difficulty performing household chores. Sometimes, she feels too fatigued to cook dinner. She has noticed that she feels better after sleeping. She does not have chest pain, shortness of breath, or a history of recent illness. She has smoked two packs of cigarettes daily for 25 years. She appears fatigued. Her temperature is 37.0°C (98.6°F), pulse is 88/min, and blood pressure is 148/80 mm Hg. Pulse oximetry shows an oxygen saturation of 98% on room air. Bilateral expiratory wheezes are heard at both lung bases. Examination shows drooping of the upper eyelids. There is diminished motor strength in the upper extremities. Sensation and reflexes are intact. A treatment that has which of the following mechanisms of action is the most appropriate next step in management?

A. Inhibition of acetylcholinesterase
B. Stimulation of β2 adrenergic receptors
C. Removal of autoantibodies, immune complexes, and cytotoxic constituents from serum
D. Reactivation of acetylcholinesterase
E. Competitive blocking of the muscarinic receptor

Explanation: In MG, acetylcholine receptor antibodies prevent acetylcholine (ACh) from docking to the ACh receptors at the neuromuscular junction. Cholinesterase inhibitors act by inhibiting the enzymatic degradation of ACh, resulting in increased availability of endogenous ACh in the synaptic cleft and improved neuromuscular transmission. Pyridostigmine and neostigmine are the preferred drugs since they only act on peripheral ACh receptors and do not cross the blood-brain barrier, thereby limiting central adverse effects. Other acetylcholinesterase inhibitors that cross the blood-brain barrier (e.g., physostigmine, rivastigmine) are used in the treatment of glaucoma or atropine overdose..

Q9 (AMBOSS): A 35-year-old woman comes to the physician because of blurred vision for the past 2 months. During this period, she has also had difficulty chewing and swallowing. She reports that her symptoms worsen throughout the day and improve with rest. There is no personal or family history of serious illness. The patient works as a teacher and has had a great deal of stress lately. Physical examination shows bilateral ptosis and mask-like facies. Muscle strength is decreased in the bilateral lower extremities. The anti-acetylcholine receptor (AChR) antibody test is positive. Electromyography shows a decremental response following repetitive nerve stimulation. Which of the following is the most appropriate next step in the management of this patient?

A. Serum ACTH and CRH levels
B. Physostigmine therapy
C. CT scan of the chest
D. Plasmapheresis
E. Acetylcholine Receptor (AChR) Antibodies testing

Explanation: CT scan of the chest is indicated in all patients with newly-diagnosed MG to rule out thymoma. > 75% of MG patients with positive AChR antibodies have thymic abnormalities. The most common abnormality is thymic hyperplasia, but thymic tumors (usually thymoma) are found in 15% of cases. Thymectomy can improve symptoms of myasthenia gravis, even in patients without thymic abnormalities. Symptomatic treatment of MG consists of cholinesterase inhibitors such as pyridostigmine. Supplemental immunosuppressants (e.g., glucocorticoids, azathioprine) can be added if symptoms persist despite anticholinesterase therapy.

Answers: Q7: D | Q8: A | Q9: C

Multiple sclerosis

Q1 (500Best): A 23-year-old woman complains that her right leg has become progressively stiff and clumsy over the last couple of weeks. She is worried as she has not been able to go to work for the last 4 days. On examination, tone is increased and there is a catch at the knee. She has six beats of clonus and an upgoing plantar. Power is reduced to 3-4/5 in the right leg flexors. There is no sensory involvement and the rest of the neurological exam is normal other than a pale disc on opthalmoscopy. On further questioning, she admits that she has had two episodes of blurred vision in her right eye in the last two years. Each lasted a couple of weeks from which she fully recovered. What is the most appropriate initial treatment?

A- A non-steroidal anti-inflammatory drug (NSAID)
B- Interferon-beta
C- Bed rest
D- Methotrexate
E- A course of oral steroids

Explanation: The subacute onset of upper motor neurone signs on a background of episodes of optic neuritis in a young woman makes relapsing–remitting MS the likely diagnosis. The diagnosis of MS hinges on the presence of multiple central nervous system (CNS) lesions separated by time and space. These manifest in either signs/symptoms or as enhancing white matter lesions on gadolinium-enhanced MRI. There is no specific role for NSAIDs in MS (A). Even if the patient complained of pain, it would be important to ensure its origin. NSAIDs would not be appropriate for neuropathic pain. This patient may be eligible for a disease-modifying drug such as interferon beta (B) or glatiramer acetate, as she has a relapsing–remitting course and recent symptoms, but this would not be the most immediate treatment. These drugs reduce the number of relapses experienced by one- third over two years and are expensive. Long-term effects on morbidity are currently unclear. Bed rest alone (C) is inappropriate as this patient would benefit from a course of steroids as she has disabling symptoms. Oral steroids (E) have been shown to be as effective as intravenous steroids, although patients tend to be admitted for IV treatment. They reduce the length of the relapse so the patient would recover quicker, but have no effect on number of relapses or accumulation of disability. There is no evidence for methotrexate (D) in relapsing–remitting MS.

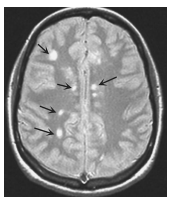
Q2 (500Best): A 42-year-old woman presents with ataxia. Gadolinium-enhanced MRI reveals multiple subcortical white matter lesions as well as enhancing lesions in the cerrebellum and spinal cord. She is diagnosed with MS. Two months later she develops optic neuritis. What feature is associated with a milder disease course?

A- Her age of 42
B- Her initial presentation of ataxia
C- Her female gender
D- The interval between the two episodes of two months
E- Her MRI scan appearance

Explanation: In this woman's case, all of the features except her gender (C) point to a more aggressive disease course. Although it is close to impossible to predict an individual patient's outcome, features of a better prognosis include onset under 25 years (A), optic neuritis or sensory, rather than cerebellar symptoms on initial presentation (B), a long interval (>1 year) between relapses (D) and few lesions on MRI (E). Full recovery from relapses is also a positive feature. Progressive MS carries a poorer prognosis compared to relapsing–remitting MS.

Q3 (Resource): A 26-year-old woman presents for follow-up of her multiple sclerosis (MS). She has had two separate episodes of optic neuritis and has noticed stutteringly progressive weakness in her lower extremities. She has a mild neurogenic bladder. Her symptoms have been stable over the past 4 months. MRI scanning reveals several plaques in the periventricular white matter (MR scan shown in the following figure) and several other plaques in the brainstem. What is the best next step in her management?

A. Intravenous methylprednisolone 1 g daily for 3 days
B. Oral cyclophosphamide
C. Oral anticholinergics for the urinary incontinence and observation of the demyelinating process
D. Interferon-beta
E. Intravenous mitoxantrone every 3 months

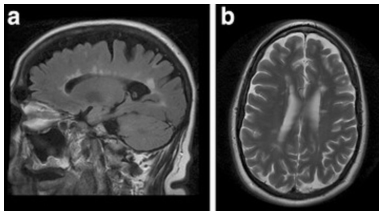


Explanation: Interferon-beta is a standard therapy used to prevent progressive disease in relapsing-remitting multiple sclerosis. Both interferon-beta 1b and several forms of interferon-beta 1a are available and are similarly effective. Glatiramer acetate (Copaxone) is also approved for MS. While patients who receive any one of these treatments have 30% fewer exacerbations, fewer new MRI lesions and less long-term disability, the treatments do not cure the disease. Interferon-beta can cause side effects, particularly a flulike syndrome that usually resolves within several months. Acute exacerbations of MS are treated with high-dose methylprednisolone followed by tapering oral prednisone. This treatment improves symptoms during a relapse but does not affect the long-term course of the disease. This patient, however, is not having an acute exacerbation of her disease. Steadily progressive MS, especially primary progressive disease, when the disease never remits but worsens inexorably, is a difficult management problem. Immunosuppressives such as cyclophosphamide and mitoxantrone are often tried. Such patients often progress to debility and mortality from urinary infection, aspiration pneumonia, or infected pressure ulcers. Providing this patient with stutteringly progressive disease with symptomatic treatment alone would be inappropriate.

Answers: Q1: E | Q2: C | Q3: D

Multiple sclerosis

Q4 (AMBOSS): A 30-year-old woman comes to the physician because of increasing weakness in both legs for 7 days. She also reports a tingling sensation in her legs that is exacerbated by taking a hot shower. She is sexually active with one male partner and does not use condoms. Her temperature is 37.8°C (100.1°F). Physical examination shows decreased muscle strength and clonus in both lower extremities. Patellar reflex is 4+ bilaterally and plantar reflex shows an extensor response on both sides. Abdominal reflex is absent. An MRI of the brain is shown. Which of the following findings is most likely to further support the diagnosis in this patient?



A- Positive antibody response to cardiolipin-cholesterol-lecithin antigen in the serum
B- Oligodendrocytes that stain positive for polyomavirus proteins on brain biops
C- Presence of immunoglobulin bands on cerebrospinal fluid immunofixation
D- Identification of gram-positive cocci in groups on blood culture
E- Detection of high-affinity antibodies to dsDNA in the serum

Explanation: The presence of immunoglobulin bands (particularly oligoclonal bands) and increased IgG production in the CSF are highly sensitive, but nonspecific, findings that support the diagnosis of MS. Lumbar puncture is indicated for patients with suspected multiple sclerosis who have inconclusive clinical and MRI findings. The production of multiple, nonspecific clones of IgG within the CNS is a result of intrathecal inflammation.

Q5 (AMBOSS): A 33-year-old woman comes to the physician for a routine health maintenance examination. She feels well. She was diagnosed with multiple sclerosis one year ago. She has had two exacerbations since then, each lasting 1 week and each requiring hospitalization for corticosteroid treatment. Her most recent exacerbation was three weeks ago. She has had no neurologic symptoms between exacerbations. She takes a multivitamin and a calcium supplement daily. Her vital signs are within normal limits. Examination, including neurologic examination, shows no abnormalities. Which of the following is the most appropriate next step in pharmacotherapy?

A- Natalizumab
B- Mitoxantrone
C- Methylprednisolone
D- Interferon beta
E- Supportive therapy only as needed

Explanation: Interferon beta can be used for the prevention of relapses in all forms of MS. Interferon beta prevents exacerbations of MS by downregulating the expression of MHC molecules on antigen-presenting cells, inhibiting T cell proliferation, and decreasing the level of proinflammatory cytokines while increasing the level of regulatory cytokines. Other drugs that can be used as first-line disease-modifying drugs in relapsing-remitting MS include glatiramer acetate, dimethyl fumarate, teriflunomide, and fingolimod.

Q6 (AMBOSS): A 25-year-old woman comes to the physician because of intermittent painful double vision for the past 3 days. Her symptoms occur only when looking sideways. She has myopia and has been wearing corrective lenses for 10 years. Ten days ago, she lost her balance and fell off her bike, for which she went to a hospital. A CT scan of the head at that time showed no abnormalities and she was released without further treatment. Her only medication is an oral contraceptive. Vital signs are within normal limits. The pupils are equal and reactive to light. Her best corrected visual acuity is 20/40 in each eye. She has an adduction deficit in the right eye and horizontal nystagmus in the left eye when looking left; she has an adduction deficit in the left eye and horizontal nystagmus in the right eye when looking right. Convergence testing shows no abnormalities. Fundoscopy shows bilateral disc hyperemia. Which of the following is the most likely cause of this patient's findings?

A. Caudal displacement of cerebellar vermis
B. Demyelination of the medial longitudinal fasciculus
C. Antibodies against acetylcholine receptors
D. Compressive tumor of the pons
E. Oxidative damage due to thiamine deficiency

Explanation: Bilateral INO, optic neuritis, and ataxia (loss of balance) in a young woman should raise concern for multiple sclerosis (MS). In MS, demyelination of the medial longitudinal fasciculus (MLF) can lead to INO. In younger patients, MS is the most common cause of INO. In older patients (especially those with arteriosclerotic risk factors), INO is more commonly caused by ischemic infarction and manifests with unilateral findings and additional stroke findings. All patients with INO should undergo MRI of the brain.

Answers: Q4: C | Q5: D | Q6: B

Multiple sclerosis

Q7 (AMBOSS): A 35-year-old woman comes to the physician for the evaluation of increasing weakness and numbness of the upper extremities for 5 days. During this time, she has also had urinary incontinence not related to sneezing or laughing. She reports that last summer during a vacation in Mexico she had weakness and numbness of her right lower extremity that was worse when she was outside; she regained her strength 3 weeks later. She has no history of serious illness. She has had 10 male sexual partners in her lifetime and uses condoms inconsistently. Vital signs are within normal limits. Examination shows an impaired tandem gait. There is mild spasticity and muscle strength is decreased in both upper extremities. Deep tendon reflexes are 4+ bilaterally. Abdominal reflex is absent. Muscle strength in the right lower extremity is mildly decreased. Sensation to vibration and fine touch is decreased over the upper extremities. Which of the following is the most appropriate next step in diagnosis?

A- Serum vitamin B12 level
B- Antinuclear antibody testing
C- Rapid plasma reagin test
D- MRI of the brain and spine
E- Lumbar puncture

Explanation: MRI of the brain and spine is the investigation of choice for a definitive diagnosis of multiple sclerosis (MS). MRI typically shows multiple asymmetric white matter lesions with finger-like radial extensions often located in the spinal cord, juxtacortical, infratentorial, and periventricular regions. If a gadolinium contrast agent is used, active lesions usually appear enhanced up to 6 weeks after exacerbations. This patient most likely has relapsing-remitting MS with symptoms that correspond to lesions in the pyramidal tracts (weakness, spasticity, increased deep tendon reflexes), dorsal spinal column (loss of vibration and fine touch), and autonomic nervous system (urinary incontinence). Absent abdominal reflex is an early and important sign of MS that is seen in about 70% of patients.

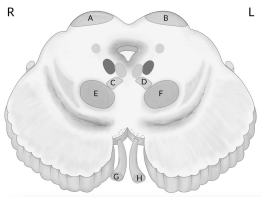
Q8 (AMBOSS): A 33-year-old woman comes to the physician because of vision impairment in her right eye for the past 2 weeks. During this period, she was unable to distinguish colors with her right eye. She also reports pain with eye movement. She has no double vision. She occasionally has headaches that are relieved with ibuprofen. One year ago, she had a similar episode that affected her left eye and resolved spontaneously. She has no history of serious illness. She works at a library and enjoys reading, even in poor lighting conditions. Her vital signs are within normal limits. The pupils are equal, round, and reactive to light and accommodation. Without correction, visual acuity is 20/50 in the left eye, and 20/100 in the right eye. With spectacles, the visual acuity is 20/20 in the left eye and 20/100 in the right eye. Slit-lamp examination shows no abnormalities. A CT scan of the head shows no abnormalities. Which of the following is the most likely diagnosis?

A- Open-angle glaucoma
B- Retinitis pigmentosa
C- Optic neuritis
D- Macular degeneration
E- Angle-closure glaucoma

Explanation: InterfThis patient's presentation is consistent with optic neuritis, which is often the first manifestation of multiple sclerosis (MS). MS is more common in women than men and it typically manifests at 20–40 years of age, with a relapsing-remitting clinical pattern. Most patients with optic neuritis have a normal fundus on ophthalmoscopy and it is not uncommon for a cranial CT to show no abnormalities, especially in the early stages of MS. All patients who present with new-onset optic neuritis should undergo a brain MRI to assess for demyelinating plaques, which support a diagnosis of MS.

Q9 (AMBOSS): A 30-year-old woman comes to the physician for the evaluation of a 2-day history of intermittent dizziness and double vision. She reports double vision whenever she looks to the left. Last summer, she had an episode of weakness in her left leg that resolved spontaneously. Ophthalmologic examination shows weak adduction of the right eye on left lateral gaze. Attempted left lateral gaze results in horizontal nystagmus of the left eye. Convergence testing is normal. This patient most likely has a lesion in which of the following labeled areas of the schematic overview of a transverse section of the midbrain?

A. A
B. B
C. C
D. D
E. E



Explanation: The medial longitudinal fasciculus (MLF) connects the nucleus of the CN VI (which controls ocular abduction) to the contralateral nucleus of the CN III (which controls ocular adduction). This connection allows for the coordination of both eyes during lateral gaze. Lesions in the MLF, such as those found in multiple sclerosis, disrupt adduction of the eye ipsilateral to the lesion, causing nystagmus in the contralateral eye as diplopia causes it to readjust..

Answers: Q4: C | Q5: D | Q9: C

General neurology

Q1 (500Best): A female presents with diplopia. On closer examination, when asked to look right, her left eye stays in the midline but her right eye moves right and starts jerking. What is the diagnosis?

A- Myasthenia gravis (MG)
B- Vertigo
C- Cerebellar syndrome
D- MS
E- Peripheral neuropathy

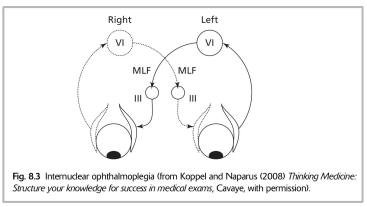


Fig. 8.3 Internuclear ophthalmoplegia (from Koppel and Naparus (2008) *Thinking Medicine: Structure your knowledge for success in medical exams*, Cavaye, with permission).

Explanation: This patient has an intranuclear opthalmoplegia (INO). This means that there is a problem in the communication between CN VI (abducens) of the right eye and CN III (occulomotor) of the left eye. Normally these nuclei communicate via the medial longitudinal fasciculus in order to maintain conjugate gaze. This keeps the eyes aligned on the same spot. If they are not aligned, double vision occurs. In this patient's case, there is a lesion in the medial longitudinal fasciculus (MLF). To look right, she abducts her right eye, but as the MLF is affected, she is unable to direct the left eye to adduct to maintain conjugate gaze. This results in diplopia. The right eye which has abducted fully develops compensatory nystagmus as the left eye has failed to adduct. Note that the problem is not in the oculomotor nerve or medial rectus. The vestibulo-occular reflex would be intact, i.e. if the patient were to keep her eyes fixed on a target and move her head left, her left eye would adduct normally. Multiple sclerosis (D) is a common cause of INO. MG (A) often results in ophthalmoplegia (paralysis of one or more extraocular muscle), but this affects the neuromuscular junction, not the MLF. Cerebellar syndromes (C) would result in nystagmus but not ophthalmoplegia. Peripheral neuropathies (E) are not directly associated with opthalmoplegia or nystagmus. Vertigo (B) is a symptom, not a diagnosis. It is the illusion of movement (i.e. a subjective sensation of movement where there is none). It is best elicited by asking the patient if they see the room moving. This clearly differentiates it from the vague report of 'dizziness' (see Figure 8.3).

Q2 (500Best): Which of the following is not a cause of absent ankle jerks and up-going plantars?

A- Freidreich's ataxia
B- B_{12} deficiency
C- MS
D- Cord compression
E-Motor neurone disease

Explanation: Causes of absent ankle jerks and upgoing plantars is a common question as it implies both upper and lower motor neuron involvement. The more common single causes include cord compression (D) involving both the cord (UMN) and nerve ganglia/roots (LMN) as well as subacute combined degeneration of the cord (B). Other more common causes include the presence of more than one pathology, e.g. stroke (UMN) with superimposed peripheral neuropathy (LMN) – usually in a diabetic patient. Motoneurone disease (E) consists of a mixture of UMN and LMN signs without any sensory involvement. In Friedrich's ataxia (A), both cord and peripheral nerve involvement accompany cerebellar degeneration. These patients also have sensory loss, pes cavus and may have complications such as diabetes and hypertrophic cardiomyopathy. Multiple sclerosis (C) may cause a mixture of pyramidal signs (UMN), sensory loss (dorsal columns) and ataxia (cerebellum), but will never involve the LMN.

Q3 (MKSAP): A 66-year-old man is evaluated in the office for a 6-month history of a resting right arm tremor. He says that his writing has gotten smaller during this time and that he has had difficulty buttoning his dress shirts. The patient reports no prior medical problems and is not aware of any neurologic problems in his family. He takes no medications.Results of a general medical examination are normal. Neurologic examination shows a paucity of facial expression (hypomimia). Cranial nerve function is normal. Motor examination shows normal strength but mild left upper limb rigidity and a 5-Hz resting tremor of the right upper limb. Deep tendon reflexes are normal, as are results of sensory examination. There is no truncal or appendicular ataxia. Diminished arm swing is noted bilaterally but is worse on the right. A tremor in the right upper limb is noted during ambulation. Left upper limb alternating motion rates are diminished. Which of the following is the most likely diagnosis?

A- Cervical dystonia
B- Essential tremor
C- Huntington disease
D- Parkinson disease

Explanation: The diagnosis of Parkinson disease is based on a cardinal set of clinical features, including resting tremor, bradykinesia, rigidity, and postural instability. The patient's findings are not compatible with cervical dystonia, essential tremor, or Huntington disease. Cervical dystonia.

Answers: Q1: D | Q2: C | Q3: D

General neurology

Q4 (MKSAP): A 34-year-old woman is evaluated in the office for right-sided facial paralysis that she noticed on awakening 1 hour ago. She has a 10-pack-year smoking history. Personal and family medical history is noncontributory. Her only medication is a daily oral contraceptive. On physical examination, vital signs are normal. Limb strength, reflexes, and tone are normal bilaterally. Findings from a sensory examination, which included her face, are also normal. When asked to raise her eyebrows, the patient does not elevate the right side. When asked to shut her eyes, she cannot close the right one but the globe rotates upward, partially covering the iris. When asked to smile, the patient does not move the right side of her face. Which of the following is the most likely diagnosis?

A- Graves ophthalmopathy
B- Left cerebral infarction
C- Right facial nerve (Bell) palsy
D- Right trigeminal neuralgia

Explanation: This patient's physical examination findings most strongly suggest right facial nerve (Bell) palsy. The precise cause of Bell palsy is not known, and it is still considered an idiopathic disorder. Research strongly suggests it may be the result of herpes simplex virus infection of the facial nerve. Bell palsy is not considered contagious. The seventh cranial nerve innervates all muscles of facial expression (the mimetic muscles). Any cause of a complete facial neuropathy will therefore impair the entire hemiface, including the forehead corrugators typically spared by cerebral lesions. Bell phenomenon describes the reflexive rolling upwards of the globe during eye closure. When a normal patient is asked to close the eyes, forced eyelid opening will reveal this phenomenon, as will the selective paralysis of the orbicularis oculi due to a facial neuropathy. Facial neuropathies will otherwise spare the extraocular muscles that govern globe movement. Because Bell palsy is a diagnosis of exclusion, clinicians need to make every effort to exclude other identifiable causes of facial paralysis, such as Lyme disease, HIV disease, acute and chronic otitis media, cholesteatoma, and multiple sclerosis. Other common causes of acute peripheral facial paralysis will often have findings on history or physical examination that suggest the correct diagnosis. Graves ophthalmopathy can cause proptosis or extraocular muscle edema with consequent eye movement abnormalities but is not associated with the facial hemiparalysis typical of facial nerve (Bell) palsy. Cerebral infarction, brain hemorrhage, or any structural brain lesion can cause weakness of the lower face but not of the forehead because the bilateral cortical representation of the midline forehead spares the forehead corrugators. Some limb or sensory abnormality is also often, but not universally, observed in the setting of cerebral infarction; no such abnormality was observed in this patient. Therefore, despite her cerebrovascular risk factors of oral contraception and cigarette smoking, this patient is unlikely to have had a cerebral infarction. The trigeminal nerve provides sensation, not movement, to the muscles of facial expression, so trigeminal neuralgia is not a likely diagnosis in this patient with normal sensation.

Q5 (MKSAP): An obese 66-year-old man has had increasing pain and tingling in his feet for more than 8 months. The patient has not seen a physician in more than 20 years. His only other symptoms are fatigue, blurry vision, and nocturia. He takes no medications. On examination, vital signs are normal; BMI is 30. Results of skin, ophthalmoscopic, cardiopulmonary, and abdominal examinations are normal. On neurologic examination, he has sensory loss in the feet and distal legs. Muscle strength and reflexes are normal. Which of the following tests will most likely diagnose the cause of the neurologic findings?

A- Creatine kinase level
B- Fasting blood glucose level
C- Lumbar puncture and cerebrospinal fluid analysis
D- Sural nerve biopsy

Explanation: The fasting blood glucose level will most likely provide a diagnosis autonomic nerves. Loss of sensation in a "stocking-glove" distribution that is associated with paresthesias or painful dysesthesias is the most common presentation of this condition. Loss of sensation in the lower extremities is typical and plays a major part in the development of foot ulcerations, which can lead to limb loss. No direct treatment for diabetic neuropathy exists, other than to improve glycemic control. Pharmacologic therapy, however, may help symptoms. Partial serotonin and norepinephrine reuptake inhibitors (duloxetine), tricyclic antidepressants (amitriptyline), and various antiseizure medications (gabapentin, phenytoin, carbamazepine) are frequently used to treat the pain associated with this condition.
Obtaining a creatine kinase level would be appropriate in someone with suspected primary muscle disease, but this diagnosis is not likely in this patient, given the presence of neuropathic pain and sensory loss without muscle weakness. Lumbar puncture and cerebrospinal fluid examination should be considered in patients with acute, severe, or rapidly progressive neuropathy and in those with a demyelinating neuropathy; in these situations, lumbar puncture may help to confirm the presence of an inflammatory process in the cerebrospinal fluid but would not result in a specific diagnosis. Multiple sclerosis, the most common example of a demyelinating disorder, is characterized by discrete subacute episodes of neurologic dysfunction that progress over days to weeks, plateau, and then improve partially or completely over subsequent days to months. Sural nerve biopsy is most typically performed in patients with suspected vasculitis or amyloidosis. Patients with vasculitic neuropathy typically have a systemic illness with manifestations in other organs, including the skin, lungs, and kidneys; vasculitic neuropathy as the sole presenting feature of a systemic illness would be very unusual. Like vasculitis, amyloidosis is a systemic disease with manifestations involving many organ systems and would not likely present with symptoms confined to the peripheral nervous system of the lower extremities.

Answers: Q4: C | Q5: B

General neurology

Q6 (pretest): A 64-year-old man is evaluated because of weakness and difficulty in weaning from mechanical ventilation. The patient had been admitted to the intensive care unit 2 weeks ago because of septic shock related to alcoholism, pneumonia, and Klebsiella bacteremia. He had developed respiratory failure requiring intubation and mechanical ventilation as well as acute kidney injury. His pulmonary infiltrates had responded to appropriate intravenous antibiotics and his hypotension had responded to intravenous norepinephrine. Now the patient is alert and responsive to verbal commands, is afebrile with blood pressure of 114/74 but has not tolerated several trials of weaning from the ventilator. On physical examination, the patient is cooperative. Cranial nerves are normal. Muscle strength is poor, especially in distal musculature, where he displays only 2/5 strength in the hands and feet. Proximal strength is 3/5. Ankle and knee reflexes are unobtainable. Sensory examination is difficult because of problems communicating with the patient but suggests distal sensory loss in the lower extremities. Laboratory studies show that his creatinine level has spontaneously improved to 2.4 mg/dL. Electrolytes are normal, and the patient has a mild normochromic normocytic anemia with resolving leukocytosis. Serum creatine kinase is 78 units/L (normal <140). What is the most likely cause of his weakness?

A. Muscle degeneration with loss of myosin in myocytes
B. Persistent neuromuscular blockade due to aminoglycoside use
C. Thiamine depletion from intravenous glucose administration
D. Axonal degeneration of peripheral nerves with denervation potentials in myocytes
E. Demyelination of peripheral nerves from unrecognized Guillain-Barré syndrome (GBS)

Explanation: This patient suffers from critical care polyneuropathy, which affects 25% to 50% of ICU patients who have suffered multiorgan failure or who have required long-term mechanical ventilation. It typically presents with motor weakness and difficulty in weaning the patient from the ventilator. Cranial nerves are spared. Distal reflex loss, sensory changes in neuropathic distribution, and normal CK help distinguish it from critical care myopathy. Both conditions can coexist in the same patient and distinction between the two conditions may not be important, as treatment of both conditions is supportive. Patients usually improve slowly with time, but prolonged dependence on the ventilator as well as weakness and sensory loss lasting months or years often occur. The cause of critical care polyneuropathy is unknown, but axonal degeneration on nerve conduction studies is characteristic. Loss of myosin characterizes the closely related condition of critical care myopathy, but sensory changes and reflex loss would not be anticipated in a myopathic process. Neuromuscular blockade again would not cause sensory and reflex changes. Thiamine deficiency can be provoked in a malnourished patient (such as one suffering from chronic alcoholism) but would be associated with nystagmus, ataxia, and mental status changes rather than distal weakness and neuropathy.Demyelination (rather than axonal degeneration) is associated with Guillain-Barré syndrome, but this condition would be very unlikely in this ICU patient without antecedent viral or Campylobacter infection.

Q7 (pretest): A 30-year-old man complains of bilateral leg weakness and clumsiness of fine movements of the right hand. Five years ago he had an episode of transient visual loss. On physical examination, there is hyperreflexia with Babinski sign in the lower extremities and cerebellar dysmetria with poor finger-to-nose movement on the right. When the patient is asked to look to the right, the left eye does not move normally past the midline. Nystagmus is noted in the abducting eye. A more detailed history suggests the patient has had several episodes of gait difficulty that have resolved spontaneously. He appears to be stable between these episodes. He has no systemic symptoms of fever or weight loss. Which of the following is the most appropriate next test to order?

A. Lumbar puncture
B. MR scan with gadolinium contrast
C. Quantitative cerebrospinal fluid (CSF) IgG levels
D. Testing for oligoclonal bands in cerebrospinal fluid
E. CT scan of the head with intravenous-iodinated contrast

Explanation: This patient's symptoms and signs are worrisome for a demyelinating process such as multiple sclerosis. The episode of transient blindness was likely a result of optic neuritis, which occurs in 25% to 40% of multiple sclerosis patients (a similar presentation can occur in systemic lupus erythematosus [SLE], sarcoidosis, or syphilis). In addition, the patient gives a history of a relapsing-remitting process. There are abnormal signs of cerebellar and upper motor neuron disease; the eye movement abnormalities indicate intranuclear ophthalmoplegia. Signs and symptoms therefore suggest multiple lesions in space and time, making multiple sclerosis the most likely diagnosis. All patients with suspected multiple sclerosis should have MR imaging of the brain. MRI is sensitive in defining demyelinating lesions in the brain and spinal cord; gadolinium infusion is necessary to demonstrate active demyelination. Disease-related changes on MRI are found in more than 95% of patients who have definite evidence for MS. Most patients do not need spinal fluid analysis for diagnosis. Although 70% will have elevated IgG levels and 85% will have oligoclonal bands on CSF analysis, lumbar puncture is reserved for cases where the diagnosis is uncertain. Finding pleocytosis of greater than 75 cells per microliter or any polymorphonuclear leukocytes in the CSF makes the diagnosis of MS unlikely. In some cases, chronic infection with syphilis or HIV may mimic MS. CT scanning is much less sensitive than MRI in detecting demyelinating lesions, especially in the posterior fossa and cervical cord.

Answers: Q6: D | Q7: B

General neurology

Q8 (pretest): A 20-year-old woman complains of weakness that is worse in the afternoon, worse during prolonged activity, and improved by rest. When fatigued, the patient is unable to hold her head up or chew her food. She often notes diplopia when driving home from work. On physical examination, she has no loss of reflexes, sensation, or coordination. Which of the following is the likely pathogenesis of this disease?

A. Autoantibodies directed against the postsynaptic acetylcholine receptor causing neuromuscular transmission failure
B. Destruction of anterior horn cells by virus
C. Progressive muscular atrophy caused by spinal degeneration
D. Demyelinating disease
E. Defect in muscle glycogen breakdown

Explanation: The disease process described is myasthenia gravis (MG), a neuromuscular disease marked by muscle weakness and fatigability. Myasthenia gravis results from a reduction in the number of junctional acetylcholine receptors as a result of autoantibodies. Antibodies cross-link these receptors, causing increased endocytosis and degradation in lysosomes. A decreased number of available acetylcholine receptors results in decreased efficiency of neuromuscular transmission. MG patients also have autoantibodies against muscle-specific tyrosine kinase (MuSK) receptors. MG presents with weakness and fatigability, particularly of cranial muscles, causing diplopia, ptosis, nasal speech, and dysarthria. Proximal limb weakness also occurs. Diseases of the central nervous system (poliomyelitis, Friedreich ataxia, or multiple sclerosis, as in answers b, c, and d) cause changes in reflexes, sensation, or coordination. ALS, a pure motor disorder, causes fasciculations and muscle atrophy as a result of lower motor neuron involvement. McArdle disease, a glycogen storage disease, causes muscle cramping and occasionally rhabdomyolysis with heavy exertion but only very rarely with usual daily activities. Ten percent of myasthenia patients have thymic tumors. Surgical removal of a thymoma is necessary because of local tumor spread. Even in the absence of tumor, 85% of patients clinically improve after thymectomy. It is common practice to perform thymectomy in most patients with generalized MG who are between puberty and age 55.

Q9 (pretest): Three weeks after an upper respiratory illness, a 25-year-old man develops weakness of his legs, which progresses over several days. On physical examination he has 4/5 strength in his arms but only 2/5 in the legs bilaterally. There is no sensory deficit, but knee and ankle reflexes cannot be elicited. During a 2-day observation period the weakness ascends, and he begins to notice increasing weakness of the hands. He notices mild tingling, but the sensory examination continues to be normal. The workup of this patient is most likely to show which of the following?

A. Acellular spinal fluid with high protein
B. Abnormal electromyogram/nerve conduction velocity (EMG/NCV) showing axonal degeneration c. Positive edrophonium (Tensilon) test
D. Elevated creatine kinase (CK)
E. Respiratory alkalosis on arterial blood gas measurement

Explanation: This patient presents with an acute symmetrical polyneuropathy characteristic of Guillain-Barré syndrome. This demyelinating process is often preceded by a viral illness or infection with Campylobacter jejuni. Characteristically, there is little sensory involvement; about 30% of patients require ventilatory assistance. Loss of deep tendon reflexes, especially in the lower extremities, is an important clue to the lower motor neuron involvement that characterizes GBS. Guillain-Barré syndrome is characterized by an elevated CSF protein with few, if any, white blood cells. EMG usually shows a demyelinating (not an axonal) process with nonuniform slowing and conduction block. A positive edrophonium test is characteristic of myasthenia gravis, but this patient's loss of tendon reflexes would not occur in MG. CK levels are normal, as there is no damage to muscle in this disease process. Arterial blood gases in Guillain Barré syndrome might show a respiratory acidosis (not respiratory alkalosis) secondary to hypoventilation.

Answers: Q8: A | Q9: A

General neurology

Q10 (pretest): A 76-year-old woman presents with numbness and mild weakness in the legs. She has noticed mild numbness in the fingertips bilaterally. The symptoms have been slowly progressive over the past year. She rarely goes to the doctor and takes no medications. Neurological examination shows sensory loss to light touch distal to the knees and wrists in a symmetric pattern. Joint position and vibratory sensation are normal. Ankle reflexes are absent, and she has mild distal weakness. Which of the following is the most likely abnormality on laboratory testing?

A. Hyperglycemia
B. Macrocytic anemia with a low vitamin B12 level
C. Oligoclonal bands on CSF analysis
D. Low T4, elevated TSH
E. Positive acetylcholine receptor antibody titers

Explanation: The disease process described is myasthenia gravis (MG), a neuromuscular disease marked by muscle weakness and fatigability. Myasthenia gravis results from a reduction in the number of junctional acetylcholine receptors as a result of autoantibodies. Antibodies cross-link these receptors, causing increased endocytosis and degradation in lysosomes. A decreased number of available acetylcholine receptors results in decreased efficiency of neuromuscular transmission. MG patients also have autoantibodies against muscle-specific tyrosine kinase (MuSK) receptors. MG presents with weakness and fatigability, particularly of cranial muscles, causing diplopia, ptosis, nasal speech, and dysarthria. Proximal limb weakness also occurs. Diseases of the central nervous system (poliomyelitis, Friedreich ataxia, or multiple sclerosis, as in answers b, c, and d) cause changes in reflexes, sensation, or coordination. ALS, a pure motor disorder, causes fasciculations and muscle atrophy as a result of lower motor neuron involvement. McArdle disease, a glycogen storage disease, causes muscle cramping and occasionally rhabdomyolysis with heavy exertion but only very rarely with usual daily activities. Ten percent of myasthenia patients have thymic tumors. Surgical removal of a thymoma is necessary because of local tumor spread. Even in the absence of tumor, 85% of patients clinically improve after thymectomy. It is common practice to perform thymectomy in most patients with generalized MG who are between puberty and age 55.

Q11 (pretest): A 58-year-old woman has a history of alcohol abuse, coronary artery disease, and atrial fibrillation. Her medications include metoprolol, lisinopril, simvastatin, and warfarin. She develops urinary urgency and frequency and is treated with oxycodone and ciprofloxacin. Three days later she develops a headache, dizziness, vomiting, and has difficulty walking. On neurological examination her strength, sensation (including vibratory sensation), and reflexes are normal. She walks with an uncoordinated, unsteady gait. On testing of coordination in the upper extremities, she displays past-pointing and poor rapid alternating movements with her right upper extremity. In the lower extremities, her heel-shin testing also reveals poor coordination on the right. INR is 6.5 (normal <1, therapeutic for warfarin 2.0-3.0). What is the most likely cause of her neurologic findings?

A. Right cerebellar hemorrhage
B. Multiple small infarcts in the basal ganglia
C. Cerebellar degeneration due to chronic alcohol abuse
D. Posterior column degeneration as a result of vitamin deficiency
E. Combined effects of oxycodone and ethanol

Explanation: This patient has evidence of cerebellar dysfunction, most likely due to cerebellar hemorrhage. Many drugs (including ciprofloxacin) interact with warfarin, excessively prolong anticoagulation, and may result in spontaneous hemorrhage. Cerebellar lesions are typically associated with ataxia and dizziness. This patient's bleeding can be localized to the right cerebellar hemisphere since a focal lesion in one lobe of the cerebellum (eg, a cerebellar tumor, hemorrhage or infarct) causes dyscoordination on the same side of the body (ipsilateral) as the lesion. Infarcts in the basal ganglia would cause extrapyramidal signs with rigidity and uncontrolled movements in addition to discoordination. Midline cerebellar lesions (most commonly alcoholic cerebellar degeneration) cause midline signs (especially gait ataxia) out of proportion to the findings in the extremities. Posterior column disease would cause sensory abnormalities (especially, loss of proprioception and vibratory sensation) rather than problems with coordination. Acute alcohol ingestion and narcotic overdose can cause dizziness and ataxia, often with nystagmus, but would not be expected to cause unilateral dysmetria.

Answers: Q10: A | Q11: A

General neurology

Q12 (pretest): A 72-year-old woman is found unconscious at home by her daughter. The daughter last spoke to her mother 1 day ago, at which time her mother seemed fine. The patient has diabetes, hypertension, atrial fibrillation, and chronic back pain. Her medications include metformin, lisinopril, warfarin, and oxycodone. On examination her blood pressure is 167/70, pulse 48 beats/min, respiratory rate 12 breaths/min and irregular, and temperature 37.2°C (98.9°F). There are no signs of trauma. Neck is supple. The patient does not respond to verbal stimuli. Pupils are equally reactive to light. The oculocephalic reflex (doll's eye maneuver) is normal. On applying firm pressure to the orbital rim, the patient flexes her right arm, but does not move her left arm. Which of the following is the most likely cause of her condition?

A. Hypoglycemia
B. Narcotic overdose
C. Lacunar infarct in the right internal capsule
D. Acute subdural hematoma
E. Anterior cerebral artery embolism

Explanation: This woman presents with coma and requires rapid and careful evaluation. The most common causes of coma are central nervous system infections (meningitis and encephalitis), structural central nervous system lesions, which produce compression of the brainstem, metabolic abnormalities, and drug overdose. The neurologic examination is very helpful in the evaluation of comatose patients, and should focus on specific maneuvers: (1) testing for nuchal rigidity, (2) pupillary response to light, (3) response to painful stimulus (typically by applying firm pressure to the sternum or orbital rim), and (4) the oculocephalic reflex (doll's eye maneuver). Neck stiffness and fever in the comatose patient would suggest meningitis or subarachnoid hemorrhage. Pupillary response to light is preserved in metabolic derangements, drug overdose, and early in space- occupying lesions. Preserved pupillary light reflex in the absence of an oculocephalic reflex is seen almost exclusively in drug overdose. In space-occupying lesions with early brainstem compression (the so-called diencephalic stage) the pupillary response to light and the oculocephalic reflex are preserved. As brainstem compression progresses to midbrain and then pons compression, pupillary response to light and the oculocephalic reflex are lost. When unilateral arm flexion with painful stimulation occurs in the comatose patient, this suggests a hemispheric mass with mild brainstem compression. As brainstem compression progresses to involve the midbrain, the comatose patient will respond to painful stimulation with arm flexion and leg extension (decorticate posturing). When brainstem compression progresses further to involve the pons, painful stimulation results in extension of both arms and legs (decerebrate posturing). This comatose patient has preserved pupillary and oculocephalic reflexes, and right arm flexion with painful stimulation. This suggests a left hemispheric space occupying lesion with early brainstem compression. The widened pulse pressure, bradycardia, and irregular breathing (Cushing reflex) also suggest increased intracranial pressure. In this patient on warfarin, these findings are likely due to an acute subdural hematoma, which may occur spontaneously or with trauma (such as falling). Emergency non-contrast CT of the head will almost always show the hematoma. Hypoglycemia is uncommon with metformin. Neither hypoglycemia nor drug overdose would cause unilateral arm flexion with painful stimulation. In the absence of fever and neck stiffness, meningitis is unlikely. A lacunar infarct will cause focal findings (such as pure motor or pure sensory stroke) but not global brain dysfunction (coma). Anterior cerebral artery occlusion causes motor and sensory deficits of the contralateral leg and foot but does not impair consciousness.

Q13 (pretest): A 73-year-old man has had three episodes of visual loss in the right eye. The episodes last 20 to 30 minutes and resolve completely. He describes the sensation as like a window shade being pulled down in front of the eye. He has a history of hypertension and tobacco use. He denies dyspnea, chest pain, palpitations, or unilateral weakness or numbness. On examination the patient appears healthy; his vital signs are normal and the neurological examination is unremarkable. An ECG shows normal sinus rhythm without evidence of ischemia or hypertrophy. Initial laboratory studies are normal. Both noncontrast CT scan of the head and MR scan of the brain are normal. What is the best next step in this patient's management?

A. Admit the patient to the hospital for intravenous unfractionated heparin.
B. Obtain an echocardiogram.
C. Check for antiphospholipid antibodies and homocysteine levels.
D. Order a carotid duplex ultrasonogram and begin antiplatelet therapy.
E. Begin lamotrigine for probable nonconvulsive seizure.

Explanation: This patient has suffered several transient ischemic attacks with the classic description of amaurosis fugax. Although the traditional symptom duration of less than 24 hours is often cited, most TIAs last less than 1 hour, usually 15 or 20 minutes. Many patients whose symptoms last for several hours are found to have ischemic strokes on MRI imaging. TIAs carry a high risk of neurological morbidity and should be promptly evaluated and treated. Five percent of patients will have a full-blown stroke within the next 2 weeks. Assessing the extracranial carotid arteries for evidence of atherosclerosis is crucial in patients with anterior circulation TIAs. If a common or internal carotid stenosis of 70% or greater is found, carotid endarterectomy has been proven to decrease the risk of subsequent stroke. Carotid angioplasty with stenting is used in some centers, but has not been studied as rigorously as carotid endarterectomy. Lesions of the external carotid artery do not cause CNS symptoms. The reason to acutely admit a patient with TIA to the hospital is to obtain rapid carotid evaluation and to evaluate for cardiac emboli. The ABCD2 system is used to stratify patients for hospital admission. Patients are given 2 points each for focal weakness (as opposed to speech or visual symptoms only) and duration of symptoms greater than 1 hour. Patients are given 1 point for age >60 years, BP above 140/90, speech impairment without weakness, duration of symptoms 10 to 59 minutes, and diabetes. Patients with an ABCD2 score of 3 or more are usually admitted for prompt evaluation. The use of anticoagulants in acute stroke has diminished greatly and is primarily used in cases of demonstrated cardiogenic emboli. For the typical atherosclerotic process, antiplatelet therapy is preferred. Cardiogenic sources of clots (ie, atrial fibrillation, mitral valve disease, intracardiac tumors) usually cause large vessel ischemic strokes rather than TIAs, so echocardiography would be less important in this patient. In addition, the normal cardiac exam and ECG make a cardiogenic source unlikely. Testing for thrombophilia is rarely helpful in patients with TIA. These tests may be helpful in patients with a large-vessel stroke and no identifiable source of the stroke. Amaurosis fugax would not be a manifestation of seizure disorder.

Answers: Q12: D | Q13: D

General neurology

Q14 (pretest): A 62-year-old man presents with several weeks of excruciating stabbing pain in his right cheek. This pain occurs several times a day, lasts for a few seconds, and is so intense that he often winces or cries out. Episodes of pain can sometimes be caused by touching the face, or by air blowing on his face. What is the most likely diagnosis?

A. Carotid artery aneurysm
B. Migraine
C. Trigeminal neuralgia
D. Glossopharyngeal neuralgia
E. Brain tumor

Explanation: Facial or head pain that is repetitive, severe, stabbing, and lasts just a few seconds is characteristic of the cranial neuralgias: trigeminal, glossopharyngeal, and occipital neuralgia. Of the cranial neuralgias, trigeminal neuralgia (tic douloureux) is the most common and typically occurs in middle-aged patients. Earlier onset can indicate underlying multiple sclerosis. The pain usually occurs unilaterally in the second or third division of the trigeminal nerve, and is classically precipitated by light touch of the face. The first-line treatment is carbamazepine, but about one-third of patients do not respond to medical treatment and require invasive management such as microvascular decompression of the trigeminal nerve. Glossopharyngeal neuralgia is much less common, is felt in the throat, and is precipitated by swallowing or yawning. In occipital neuralgia the episodes of pain originate from the base of the skull. Headaches associated with migraine tend to be throbbing and last for hours at a time. Headaches associated with brain tumors are steadily progressive and are often made worse by Valsalva maneuver and by recumbency (ie, typically worse at night). Carotid artery aneurysms may cause stroke or facial swelling but rarely cause headache.