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Residency In-service Training Examination

Discussion and Reference Manual

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Anatomy

Question 5: Anatomy - Peripheral Nervous System

Discussion:

The parasympathetic nervous system governs pupil constriction, bronchoconstriction, detrusor contraction and sphincter relaxation, and penile erections.

References:

Campbell WW. DeJong's the neurologic examination. Philadelphia: Lippincott, Williams & Wilkins, 2005.

Question 6: Anatomy - Cortex and Connections

Discussion:

The orbitofrontal syndrome consists of socially inappropriate behaviors as well as poor impulse control with disinhibition. The lateral convexity syndrome is associated with dysexecutive symptoms. The mesial frontal syndrome is associated with amotivation.

References:

Campbell WW. DeJong's the neurologic examination. Philadelphia: Lippincott, Williams & Wilkins, 2005.

Cummings JL, Mega MS. Neuropsychiatry and behavioral neuroscience. New York: Oxford University Press, 2003.

Question 7: Anatomy - Cranial Nerves

Discussion:

This patient presents with a combination of optic nerve dysfunction and ocular motility deficits. The oculomotor, trochlear, and abducens nerves all traverse through the cavernous sinus and superior orbital fissure into the orbital apex. The optic leaves the orbital apex through the optic canal and does not run through the cavernous sinus. In this context, the combination of optic nerve dysfunction and ocular motility deficits localizes to the orbital apex.

References:

Wilson-Pauwels L, Akesson E, Stewart P. Cranial nerves: anatomy and clinical components. Toronto: BC Decker Inc, 1988.

Blumenfeld H. Neuroanatomy through clinical cases. 1st ed. Sunderland: Sinauer Associates, 2002.

Question 12: Anatomy - Basal Ganglia and Thalamus

Discussion:

Thalamic astasia is characterized by an alert and awake patient with normal strength who cannot stand and sometimes sit unassisted for several days after an acute stroke. The patient may have varying degrees of sensory loss. They typically fall backwards or to the side opposite of the lesion. Lesions of the subthalamic nucleus are typically associated with hemiballismus, and putaminal lesions are often associated with weakness and chorea. Injury to the vestibular nucleus typically results in nystagmus and a tendency to fall toward the side of the lesion. Cortical areas critical for gait include the medial frontal region, the paracentral lobule, and the supplementary motor cortex.

References:

Brazis PW, Masdeu JC, Biller J. Localization in clinical neurology. 6th ed. Philadelphia: Lippincott, Williams & Wilkins, 2011.

Question 21: Anatomy - Cortex and Connections

Discussion:

Fifty patients with elevations of serum cardiac troponin levels had strokes involving the right posterior, superior medial insula, and the right inferior parietal lobule. Among patients with right middle cerebral artery strokes, the insular cortex was involved in 88% of patients with elevated serum cardiac troponin but in only 33% of patients without the elevation.

References:

Ay H, Koroshetz WJ, Benner T, et al. Neuroanatomic correlates of stroke-related myocardial injury. Neurology 2006; 66: 1325-1329.

Question 29: Anatomy - Peripheral Nervous System

Discussion:

The biceps are innervated by the musculocutaneous nerve, which arises from the lateral cord of the brachial plexus. The pronator teres is innervated by the median nerve from axons that travelled in the lateral cord of the brachial plexus. The deltoid is innervated by the axillary nerve, which arises from the posterior cord of the brachial plexus. The brachioradialis is innervated by the radial nerve, which arises from the posterior cord of the brachial plexus. The rhomboid receives supply directly from the C5 root. The supraspinatus is innervated by the suprascapular nerve, which arises from the upper trunk of the brachial plexus.

References:

Preston DC, Shapiro BE. Electromyography and neuromuscular disorders: clinical-electrophysiologic correlations. 3nd ed. Philadelphia: Elsevier, 2012.

Question 40: Anatomy - Basal Ganglia and Thalamus

Discussion:

The caudate and the putamen serve as the primary input nuclei for the basal ganglia. The globus pallidus, which projects to the ventral anterior nucleus of the thalamus, is the primary output nucleus. The substantia nigra pars compacta, located in the midbrain, sends dopaminergic fibers to the putamen. The subthalamic nucleus receives inhibitory input from the external part of the globus pallidus and sends excitatory input to the globus pallidus pars interna.

References:

Carpenter M, Sutin J. Human neuroanatomy. 8th ed. Baltimore: Williams and Wilkins, 1983.

Blumenfeld H. Neuroanatomy through clinical cases. 1st ed. Sunderland: Sinauer Associates, 2002.

Question 45: Anatomy - Cranial Nerves

Discussion:

This patient presents with a pupil-sparing third nerve palsy. The oculomotor nerve innervates the medial, superior, and inferior recti, the inferior oblique, and levator palpebrae muscles. In ischemic third nerve palsies, the pupil is typically spared, as is the periphery of the nerve, where the pupillomotor fibers course. In contrast, posterior communicating artery aneurysms typically cause third nerve palsies involving the pupil, as they compress the nerve, and therefore the peripheral pupillomotor fibers.

References:

Blumenfeld H. Neuroanatomy through clinical cases. 1st ed. Sunderland: Sinauer Associates, 2002.

Question 48: Anatomy - Brainstem/Cerebellum

Discussion:

This patient's eye movements are consistent with the "one-and-a-half" syndrome in which the ipsilateral eye has no horizontal movements and the contralateral eye is only able to abduct. The clinical findings are a combination of a left intranuclear ophthalmoplegia (which prevents the left eye from adducting on rightward gaze with end-gaze nystagmus of the abducting right eye) and a left abducens nuclear palsy (which produces an ipsilateral gaze palsy preventing the patient from looking left). The only horizontal eye movement still possible, then, is abduction of the right eye on rightward gaze. This lesion must involve the left medial longitudinal fasciculus and left abducens nucleus.

References:

Carpenter M, Sutin J. Human neuroanatomy. 8th ed. Baltimore: Williams and Wilkins, 1983.

Blumenfeld H. Neuroanatomy through clinical cases. 1st ed. Sunderland: Sinauer Associates, 2002.

Question 69: Anatomy - Cortex and Connections

Discussion:

Fibers in the inferior aspect of the retina detect vision in the superior quadrants. After synapsing in the lateral geniculate, those fibers enter the temporal lobe as Meyer's loop, and project to the occipital lobe. The superior visual fields project to the inferior lip of the contralateral calcarine sulcus.

References:

Campbell WW. DeJong's the neurologic examination. Philadelphia: Lippincott, Williams & Wilkins, 2005.

Question 82: Anatomy - Cranial Nerves

Discussion:

When the eye is abducted, the primary depressor is the inferior rectus. When the eye is adducted, the superior oblique and inferior rectus depress the eye. When the patient looks down and to the left, she is primarily using the right superior oblique and left inferior rectus.

References:

Campbell WW. DeJong's the neurologic examination. Philadelphia: Lippincott, Williams & Wilkins, 2005.

Question 89: Anatomy - Basal Ganglia and Thalamus

Discussion:

Cheiro-Oral Syndrome is a lacunar syndrome characterized by contralateral sensory deficits of the mouth and hand. It typically localizes to the VPM and VPL in the thalamus.

References:

Shirish Satpute, D.O., John Bergquist, M.S., and John W. Cole, M.D., M.S.. Cheiro-Oral Syndrome Secondary to Thalamic Infarction: A Case Report and Literature Review.

Question 92: Anatomy - Spinal Cord

Discussion:

On the ipsilateral side of a spinal cord hemisection there would be an upper motor neuron syndrome, greatly impaired discriminatory tactile sense, and reduced muscle tone below the level of the lesion. Contralateral to the lesion there would be loss of pain and temperature due to interruption of the ascending spinothalamic tracts (which cross soon after entry)

References:

Haines DE. Fundamental neuroscience. 2nd ed. New York: WB Saunders, 2002.

Question 107: Anatomy - Peripheral Nervous System

Discussion:

The short head of the biceps femoris is the only muscle proximal to the knee innervated by the peroneal division of the sciatic nerve. Needle EMG abnormalities of this muscle would indicate that a lesion of the peroneal nerve would have to be proximal to the fibular head.

References:

Campbell WW. DeJong's the neurologic examination. Philadelphia: Lippincott, Williams & Wilkins, 2005.

Question 109: Anatomy - Brainstem/Cerebellum

Discussion:

Auditory fibers from the superior olivary nucleus ascend in the lateral lemniscus to reach the inferior colliculus. The electrical activation of the lateral lemniscus is reflected in wave 4 of a brainstem auditory evoked potential. The fibers in the trapezoid body arise from the ventral cochlear or the superior olivary nucleus and decussate to the contralateral side.

References:

Carpenter MB. Core text of neuroanatomy. Baltimore: William & Wilkins, 1991.

Question 111: Anatomy - Brainstem/Cerebellum

Discussion:

Palatal myoclonus or palatal tremor is characterized by rhythmic jerking movements of the palate and pharyngeal structures that persist during sleep. It is associated with lesions that interrupt the dentato-rubro-olivary pathway, also known as the Guillain-Mollaret triangle. This triangle begins in the inferior olive, which projects via the inferior cerebellar peduncle to the contralateral dentate nucleus. It may be associated with jerky movements of the extraocular muscles, diaphragm, head, and neck. The dentate nucleus projects via the superior cerebellar peduncle to the ipsilateral red nucleus. The ipsilateral red nucleus completes the triangle by projecting to the ipsilateral inferior olive via the central segmental tract. This patient's dysarthria is likely caused by involvement of the nucleus ambiguous which provides axons to both the glossopharyngeal and vagus nerves but the nerve themselves are not the site of this patient's lesion.

References:

Brazis PW, Masdeu JC, Biller J. Localization in clinical neurology. 6th ed. Philadelphia: Lippincott, Williams & Wilkins, 2011.

Question 117: Anatomy - Cranial Nerves

Discussion:

Fibers carrying information from the temporal visual field cross in the optic chiasm. Fibers carrying information from the superior temporal visual field briefly bend up into the contralateral optic nerve (Willebrand's Knee). A lesion of the optic nerve as it joins the optic chiasm therefore interrupts all the fibers from the ipsilateral eye as well as the crossing fibers from the contralateral superior temporal visual field. This would cause the complete vision loss on the right and the left temporal hemianopsia.

References:

Blumenfeld H. Neuroanatomy through clinical cases. 1st ed. Sunderland: Sinauer Associates, 2002.

Question 122: Anatomy - Peripheral Nervous System

Discussion:

The superior gluteal nerve innervates tensor fascia latae, as well as gluteus medius and minimus. The superior gluteal nerve arises from the lumbosacral plexus. The tensor fascia latae is primarily an L5-innervated muscle and thus clinical weakness or denervation on EMG of the tensor fascia latae can be used to exclude a lesion distal to the lumbosacral plexus, such as a sciatic neuropathy.

References:

Perotto A. Anatomical guide for the electromyographer. Springfield: Charles C. Thomas, 1994.

Question 156: Anatomy - Blood Supply of Brain/Spinal Cord

Discussion:

The lateral inferior or caudal pontine syndrome due to occlusion of the anterior inferior cerebellar artery (AICA syndrome) involves lesions in the fascicles of cranial nerve VII, the spinal tract, and nucleus of cranial nerve V, the lateral spinal thalamic tract, descending sympathetic fibers (lateral reticular nucleus), the middle cerebellar peduncle, the inferior surface of the cerebellum, and in addition, the inner ear and cochlear nerve due to occlusion of the labyrinthine artery, a common branch of the AICA. Clinical findings include ipsilateral ataxia, loss of pain and temperature sensation of the face, Horner syndrome, deafness, and contralateral pain and temperature loss of the limbs.

References:

Campbell WW. DeJong's the neurologic examination. Philadelphia: Lippincott, Williams & Wilkins, 2005.

Question 158: Anatomy - Spinal Cord

Discussion:

The ciliospinal (pupillary-skin) reflex refers to pupillary dilation in response to painful stimulation. The afferent limb depends upon where the painful stimulation arises from: face (trigeminal nerve) or body (spinothalamic tract). The efferent limb of the ciliospinal reflex is carried by the third order sympathetic neurons on the common carotid artery and internal carotid artery.

References:

Arslan O. Neuroanatomical basis of clinical neurology. New York: The Parthenon Publishing Group, 2001.

Question 160: Anatomy - Embryology

Discussion:

Three embryonic communications between the vertebrobasilar and carotid systems are the trigeminal, otic and hypoglossal arteries. Persistence of the trigeminal artery is the most common.

References:

Dimmick SJ, Faulder KC.. Normal variants of the cerebral circulation at multidetector CT angiography.. Radiographics. 2009 Jul-Aug;29(4):1027-43.

Salas E, Ziyal I, Sekhar L, Wright D.. Persistent Trigeminal Artery: An Anatomic Study. Neurosurgery: 1998; Volume 43 - Issue 3 - pp 557-561

Question 162: Anatomy - Cranial Nerves

Discussion:

The motor and parasympathetic portions of CN VII pass through the geniculate ganglion without synapsing. The superior salivatory nucleus gives rise to preganglionic autonomic fibers. The sphenopalatine ganglion contains the cell bodies of the postganglionic fibers for lacrimation. Sensory fibers originating from the external auditory canal and tympanic membrane as well as fibers conveying taste have cell bodies that reside in the geniculate ganglion.

References:

Campbell WW. DeJong's the neurologic examination. Philadelphia: Lippincott, Williams & Wilkins, 2005.

Question 178: Anatomy - Spinal Cord

Discussion:

The pattern of bilateral upper extremity weakness, affecting distal muscles more than proximal ones, with decreased pinprick sensation and retained fine touch, (i.e. a dissociated sensory level in a "cape-like" distribution) is most suggestive of a central cord syndrome. A central cord lesion affecting the anterior commissure will affect the crossing spinothalamic tracts, resulting in sensory deficits only at the level of the lesion. It will not cause more caudal sensory deficits and will spare vibration and light touch, since the dorsal columns are spared.

References:

Campbell WW. DeJong's the neurologic examination. Philadelphia: Lippincott, Williams & Wilkins, 2005.

Brazis PW, Masdeu JC, Biller J. Localization in clinical neurology. 6th ed. Philadelphia: Lippincott, Williams & Wilkins, 2011.

Question 187: Anatomy - Blood Supply of Brain/Spinal Cord

Discussion:

Venous blood of the torcula exit the skull via the transverse sinus, then the sigmoid sinus, and then the jugular vein

References:

Blumenfeld H. Neuroanatomy through clinical cases. 1st ed. Sunderland: Sinauer Associates, 2002.

Question 189: Anatomy - Peripheral Nervous System

Discussion:

The inability to grip a card or paper between the thumb and index finger indicates weakness of thumb adduction and index finger abduction. Both of these muscles are innervated by the ulnar nerve. This is often called Froment sign or Froment prehensile thumb sign. The patient attempts to compensate by flexing the distal thumb and index finger making an OK sign. These muscles are innervated by the anterior interosseous nerve.

References:

Brazis PW, Masdeu JC, Biller J. Localization in clinical neurology. 6th ed. Philadelphia: Lippincott, Williams & Wilkins, 2011.

Question 190: Anatomy - Peripheral Nervous System

Discussion:

The median nerve has motor branches to lumbricals 1 and 2, the abductor pollicis brevis, the opponens pollicis brevis, and the flexor pollicis brevis, distal to the carpal tunnel.

References:

Campbell WW. DeJong's the neurologic examination. Philadelphia: Lippincott, Williams & Wilkins, 2005.

Question 192: Anatomy - Blood Supply of Brain/Spinal Cord

Discussion:

The third order neurons of the oculosympathetic pathway arise from the superior cervical ganglion on the common carotid artery. A dissection of the internal carotid artery may result in an ipsilateral Horner syndrome with ptosis, and a miotic pupil that poorly dilates. The fibers destined for the facial sweat glands are carried on the external carotid artery and therefore would be spared.

References:

Campbell WW. DeJong's the neurologic examination. Philadelphia: Lippincott, Williams & Wilkins, 2005.

Question 223: Anatomy - Brainstem/Cerebellum

Discussion:

The third cranial nerve emerges from the midbrain at the level of the superior colliculus in the interpeduncular fossa.

References:

Wilson-Pauwels L, Akesson E, Stewart P. Cranial nerves: anatomy and clinical components. Toronto: BC Decker Inc, 1988.

Carpenter M, Sutin J. Human neuroanatomy. 8th ed. Baltimore: Williams and Wilkins, 1983.

Question 224: Anatomy - Basal Ganglia and Thalamus

Discussion:

The structure is the substantia nigra, which projects to and receives fibers predominantly from the caudate and putamen. Degeneration of this structure is seen in idiopathic Parkinson's disease.

References:

Parent A. Carpenter's human neuroanatomy. 9th ed. Baltimore: Williams & Wilkins, 1996.

Haines DE. Fundamental neuroscience. 2nd ed. New York: WB Saunders, 2002.

Blumenfeld H. Neuroanatomy through clinical cases. 1st ed. Sunderland: Sinauer Associates, 2002.

Question 251: Anatomy - Spinal Cord

Discussion:

The arrow is pointing to the anterior commissure of the spinal cord, which is where the fibers of the anterolateral system, carrying pain and temperature, decussate.

References:

Haines DE. Neuroanatomy: an atlas of structures, sections and systems. 2nd ed. Baltimore: Urban & Schwarzenberg, 1987.

Nolte J. The human brain. 4th ed. St Louis: Mosby, 1999.

Question 295: Anatomy - Basal Ganglia and Thalamus

Discussion:

The marked structure is the lateral geniculate nucleus, which receives visual input from the optic tract.

References:

Haines DE. Neuroanatomy: an atlas of structures, sections and systems. 2nd ed. Baltimore: Urban & Schwarzenberg, 1987.

Nolte J. The human brain. 4th ed. St Louis: Mosby, 1999.

Question 300: Anatomy - Embryology

Discussion:

Neural crest derivatives include cells of the dorsal root ganglia (involved in transmission of pain) and sympathetic ganglia. These derivatives require nerve growth factor (NGF) for survival. Other neural crest derivatives are Schwann cells and melanocytes.

References:

Benarroch EE, Westmoreland BF, Daube JR, et al. Medical neurosciences--an approach to anatomy, pathology and physiology by systems and levels. 4th ed. New York: Lippincott, Williams & Wilkins, 1999.

Question 307: Anatomy - Cortex and Connections

Discussion:

The arcuate fasciculus is a connection between Wernicke's area in the superior temporal gyrus and Broca's area in the inferior frontal gyrus. The inferior frontal gyrus can be subdivided into three parts: pars opercularis, pars triangularis, and pars orbitalis with the first two being the anatomical substrate for Broca's area.

References:

Kandel ER, Schwartz JH, Jessel TM. Principles of neural science. 4th ed. New York: McGraw-Hill, 2000.

Carpenter MB. Core text of neuroanatomy. Baltimore: William & Wilkins, 1991.

Blumenfeld H. Neuroanatomy through clinical cases. 1st ed. Sunderland: Sinauer Associates, 2002.

Question 314: Anatomy - Cortex and Connections

Discussion:

After global brain ischemia, damage may be seen most conspicuously in parts of the cerebral cortex, hippocampus and the cerebellar Purkinje cells. In the neocortex, layer 3 is the most vulnerable to global ischemic injury, with layers 2 and 4 the most resistant. The reason for this selective vulnerability is unknown.

References:

Aminoff MJ, Greenberg DA, Simon RP. Clinical neurology. 6th ed. New York: Lange Medical Books/McGraw-Hill, 2005;225-226.

Question 322: Anatomy - Cranial Nerves

Discussion:

Innervation of the dura within the cranial vault is provided by the ophthalmic branch of the trigeminal nerve. The greater occipital nerve innervates the scalp on the back of the head. The greater petrosal nerve innervates the lacrimal gland. The maxillary and mandibular divisions of the trigeminal nerve innervate the skin of the face below the eyes.

References:

Wilson-Pauwels L, Akesson E, Stewart P. Cranial nerves: anatomy and clinical components. Toronto: BC Decker Inc, 1988.

Nolte J. The human brain. 4th ed. St Louis: Mosby, 1999.

Question 342: Anatomy - Brainstem/Cerebellum

Discussion:

Sympathetic fibers descending in the lateral dorsal medulla, lie in close approximation to the inferior cerebellar peduncle, nucleus ambiguous, fibers from the dorsal motor nucleus of X, vestibular nuclei, spinothalamic tract, and spinal trigeminal nucleus. These structures are supplied by the posterior inferior cerebellar artery and are involved in a Wallenberg syndrome.

References:

Campbell WW. DeJong's the neurologic examination. Philadelphia: Lippincott, Williams & Wilkins, 2005.

Question 349: Anatomy - Basal Ganglia and Thalamus

Discussion:

The infundibulum carries compounds from the hypothalamus to the neurohypophysis and adenohypophysis modulating the activities of these structures. The hypothalamic derived compound that tonically inhibits pituitary gland synthesis and release of prolactin is dopamine (also known as prolactin inhibitory factor). Regulation of other pituitary gland hormones is under positive control (i.e., hormone releasing factors) that are proteins. Interruption of the infundibulum leads to loss of tonic inhibition of prolactin secretion by dopamine and elevation of prolactin. Similarly, dopamine receptor antagonists will elevate prolactin and

dopamine receptor agonists can suppress prolactin secretion and have been used in the medical management of prolactin secretion pituitary adenomas.

References:

Kandel ER, Schwartz JH, Jessel TM. Principles of neural science. 4th ed. New York: McGraw-Hill, 2000.

Question 351: Anatomy - Blood Supply of Brain/Spinal Cord

Discussion:

Fetal posterior cerebral artery is a common vascular anomaly, where the distal PCA is supplied by the internal carotid artery, with an absent P1 segment. In this setting, the PCA territory is supplied by the anterior circulation; thus, internal carotid artery lesions can be responsible for PCA strokes.

References:

Stephen L. Lambert, BS,1 Frank J. Williams, MD,2 Zhora Z. Oganisyan, MD,2 Lionel A. Branch, MD,2 and Edward C. Mader, Jr, MD2. Fetal-Type Variants of the Posterior Cerebral Artery and Concurrent Infarction in the Major Arterial Territories of the Cerebral Hemisphere.

Question 352: Anatomy - Brainstem/Cerebellum

Discussion:

Decerebrate posturing is due to dysfunction of the red nucleus and the rubrospinal tract with preserved function of the lateral vestibular nucleus and the lateral vestibular spinal tracts. The rubrospinal tract facilitates motor neurons in the cervical cord subserving flexor muscles of the upper extremities. The lateral vestibulospinal tract facilitates motor neurons in the lumbosacral cord subserving extensor muscles of the lower extremities.

References:

Carpenter MB. Core text of neuroanatomy. Baltimore: William & Wilkins, 1991.

Campbell WW. DeJong's the neurologic examination. Philadelphia: Lippincott, Williams & Wilkins, 2005.

Question 364: Anatomy - Peripheral Nervous System

Discussion:

Entrapment of the suprascapular nerve may cause shoulder pain, weakness of shoulder abduction, and sparing of sensation about the shoulder. The axillary nerve supplies sensation to the skin overlying the lateral deltoid.

References:

Devinsky O, Feldmann E. Examination of the cranial and peripheral nerves. New York: Churchill Livingston, 1998.

Question 372: Anatomy - Basal Ganglia and Thalamus

Discussion:

The pulvinar receives fibers from the superior colliculus and projects to areas 17, 18 and 19. Both the inferior and lateral pulvinar have reciprocal connections with the occipital cortex. The medial geniculate receives input from the inferior colliculus while the ventral anterior nucleus receives input from the globus pallidus pars interna - particularly the non-motor information stream. The ventral posteromedial and posterolateral nuclei receive somatosensory input. The lateral dorsal nucleus has connections similar to those of the anterior nucleus to which it is adjacent though it may also have posterior parietal connections as well.

References:

Parent A. Carpenter's human neuroanatomy. 9th ed. Baltimore: Williams & Wilkins, 1996.

Blumenfeld H. Neuroanatomy through clinical cases. 1st ed. Sunderland: Sinauer Associates, 2002.

Question 376: Anatomy - Peripheral Nervous System

Discussion:

The innervation for the deltoid, biceps, brachialis, brachioradialis, supraspinatus and infraspinatus muscles are all derived from C5 and C6 myotomes and the upper trunk of the brachial plexus. The brachioradialis is innervated by the radial nerve which is derived from the posterior cord. Therefore, a lateral cord injury would spare this muscle. Nerves for the rhomboid (usually) and serratus anterior arise from the anterior primary rami and would therefore be spared in a lesion of the upper trunk.

References:

Perotto AO. Anatomical guide for the electromyographer. 3rd ed. Springfield, Illinois: Charles C Thomas Publisher, 1994.

Question 383: Anatomy - Blood Supply of Brain/Spinal Cord

Discussion:

Spinal cord infarction secondary to anterior spinal artery (ASA) occlusion is a known complication of abdominal aortic surgery. ASA syndromes present with bilateral weakness and loss of temperature and pinprick sensation below the level of the lesion.

References:

Novy J, Carruzzo A, Maeder P, Bogousslavsky J. Spinal cord ischemia: clinical and imaging patterns, pathogenesis, and outcomes in 27 patients..

Question 393: Anatomy - Spinal Cord

Discussion:

The sacral parasympathetic nucleus, located in the intermediolateral cell column at S2-S4 levels of the spinal cord, contains the preganglionic parasympathetic neurons innervating the bladder detrusor muscle. A lesion of the sacral parasympathetic nucleus can result in a hypotonic bladder. The nucleus of Onufrowicz in the S2-4 anterior horn innervates the voluntary muscle of the external urethral sphincter. A lesion of the nucleus of Onufrowicz would cause loss of external sphincter control but normal bladder contraction. A lesion of the S2-4 nerve roots would cause dysfunction of both the parasympathetic neurons to the detrusor muscle and the voluntary motor neurons to the external sphincter as seen in this patient. An injury to the thoracic spinal cord reduces the inhibition of the detrusor stretch reflex. In this setting small changes in bladder volume causes reflexive bladder contraction (spastic bladder).

References:

Brazis PW, Masdeu JC, Biller J. Localization in clinical neurology. 6th ed. Philadelphia: Lippincott, Williams & Wilkins, 2011.

Blumenfeld H. Neuroanatomy through clinical cases. 1st ed. Sunderland: Sinauer Associates, 2002.

Question 394: Anatomy - Peripheral Nervous System

Discussion:

The flexor digitorum profundus and flexor pollicis longus are innervated by the anterior interosseous nerve, a branch of the median nerve. These are the muscles required to make the OK sign with the hands. Ulnar nerve injuries typically impair pincher

grip and ability to cross 3rd digit over index finger. Radial nerve injuries typically affect the ability to extend the thumb as in hitchhiking and extend the fingers to perform a peace sign.

References:

Brazis PW, Masdeu JC, Biller J. Localization in clinical neurology. 6th ed. Philadelphia: Lippincott, Williams & Wilkins, 2011.

Behavioral/Psychiatry

Question 2: Behavioral/Psychiatry - Psychopharmacology

Discussion:

Choice of an antidepressant for an individual is based on the side effect profile of the medication and how it fits with the patient's needs. Mirtazapine is an antidepressant that promotes weight gain and helps with sleep. Both are important for this individual. Paroxetine often results in weight gain, but it can also cause insomnia. The most commonly observed adverse events consistently associated with the use of Bupropion are dry mouth and insomnia while weight is not usually affected. Sertraline typically does not cause weight gain and insomnia occurs with about the same frequency as somnolence. Insomnia and anorexia are more typical adverse events with imipramine than weight gain or sleepiness.

References:

http://www.pdr.net/.

Question 3: Behavioral/Psychiatry - Genes, Biomarkers, & Networks

Discussion:

This woman has typical features of a rapidly progressive dementia which raise the suspicion for Creutzfeldt-Jakob disease (CJD). Sporadic CJD is seen in 85-90% of cases. There are six clinical phenotypes in sporadic CJD. Familial CJD is seen in 10-15% CJD of cases. Clusters of CJD cases are usually familial. Transmitted (iatrogenic) CJD can occur via the transfer of human tissues, CSF, or blood contaminated with prion proteins (e.g. corneal transplant, neurosurgical equipment without sufficient sterilization, administration of contaminated growth hormone, or blood). These cases are very rare. Variant CJD (vCJD) is also a rare form caused by dietary consumption of beef that contains brain or spinal cord tissue infected with the prion responsible for bovine spongiform encephalopathy (BSE). Trauma can lead to Chronic Traumatic Encephalopathy (CTE), a progressive neurodegenerative condition that has a very slow progression over years.

References:

Parchi P, Strammiello R, Notari S, Giese A, Langeveld JP, Ladogana A, Zerr I, Roncaroli F, Cras P, Ghetti B, Pocchiari M, Kretzschmar H, Capellari S.. Incidence and spectrum of sporadic Creutzfeldt-Jakob disease variants with mixed phenotype and co-occurrence of PrPSc types: an updated classification.. Acta Neuropathol 2009 Nov;118(5):659-71.

Brown K, Mastrianni JA. The prion diseases. J Geriatr Psychiatry Neurol 2010 Dec;23(4):277-98

Question 8: Behavioral/Psychiatry - Language Disorders

Discussion:

This patient's main progressive deficit is limited to language that is best categorized as a Primary Progressive Aphasia (PPA). This patient's subtype is the nonfluent/agrammatic variant as this patient exhibited agrammatism with broken sentences and missing words in emails. In contrast, patients with the logopenic variant of primary progressive aphasia show impaired single-word retrieval in spontaneous speech and naming, impaired repetition of sentences and phrases, and an absence of frank agrammatism.

References:

Gorno-Tempini ML, Hillis AE, Weintraub S, Kertesz A, Mendez M, Cappa SF, Ogar JM, Rohrer JD, Black S, Boeve BF, Manes F, Dronkers NF, Vandenberghe R, Rascovsky K, Patterson K, Miller BL, Knopman DS,. Classification of primary progressive aphasia and its variants.. Neurology 2011;76(11):1006-14

Question 15: Behavioral/Psychiatry - Psychopharmacology

Discussion:

Well-known side effects of lithium therapy include dyspepsia, nausea, vomiting, diarrhea, hair loss, acne, tremor, decreased cognition, and incoordination. Lithium is used to treat episodes of mania, but mania is not a side-effect.

References:

Stahl SM. Stahl's essential psychopharmacology. 3rd ed. New York: Cambridge University Press, 2008.

Question 18: Behavioral/Psychiatry - Anatomic syndromes

Discussion:

Anosognosia (unawareness of deficit or illness) is usually seen associated with nondominant parietal lobe lesions. Achromatopsia is found after lesions of the inferior lip of the occipital lobe. Limb kinetic apraxia is seen after lesions of the anterior corpus callosum. Expressive aprosodia is seen after right frontal lesions. Semantic aphasia is seen after dominant hemisphere lesions.

References:

Feinberg TE, Farah MJ. Behavioral neurology and neuropsychology. 2nd ed. New York: McGraw-Hill, 2003.

Question 36: Behavioral/Psychiatry - Dementia

Discussion:

Early manifestations of Lewy Body Dementia reflect deficits in executive dysfunction (like attention, judgement and decision making), visuospatial processing, hallucinosis and disordered sleep. Other more general features of cognitive decline, and mood changes generally occur later. Gait and memory impairment are more common in normal pressure hydrocephalus. Behavioral changes and disinhibition are more common in frontotemporal dementia. Apraxia is associated with lesions of the dominant parietal lobe. Aphasia is more common with the language predominant dementias like semantic dementia and primary progressive aphasia. Depression is common in all neurodegenerative disease.

References:

McKeith IG1, Boeve BF2, Dickson DW2, Halliday G2, Taylor JP2, Weintraub D2, Aarsland D2, Galvin J2, Attems J2, Ballard CG2, Bayston A2, Beach TG2, Blanc F2, Bohnen N2, Bonanni L2, Bras J2, Brundin P2,. Diagnosis and management of dementia with Lewy bodies: Fourth consensus report of the DLB Consortium.. Neurology. 2017 Jun 7. pii: 10.1212/WNL.0000000000004058. doi: 10.1212/WNL.0000000000004058. [Epub ahead of print]

Moore, DP and Puri, BK. Textbook of Clinical Neuropsychiatry and Behavioral Neuroscience.

Question 55: Behavioral/Psychiatry - General Psychiatry

Discussion:

A diagnosis of major depression requires the presence of five out of nine depressive symptoms listed in DSM V for at least two weeks. The diagnosis suggests a biologic pathophysiology and is usually an indication for pharmacologic intervention.

References:

American Psychiatric Association. Diagnostic and statistical manual of mental disorders (DSM-5). 5th ed. Arlington, VA: American Psychiatric Association, 2013.

Question 56: Behavioral/Psychiatry - Psychopharmacology

Discussion:

Dopaminergic agonists and inhibitors of dopamine reuptake have been used to treat the behavioral traits associated with medial frontal syndrome. Methylphenidate is such a drug. This syndrome may be seen after ischemia in the distribution of the anterior cerebral artery.

References:

Cummings JL, Mega MS. Neuropsychiatry and behavioral neuroscience. New York: Oxford University Press, 2003.

Question 62: Behavioral/Psychiatry - Dementia

Discussion:

Typical features of early Alzheimer disease include impaired insight, disorientation to day and date, memory loss, and constructional impairments. Frontotemporal dementia patients have poor insight, but memory and especially visual-spatial abilities are not impaired as early as in Alzheimer disease. Dementia of depression, Parkinson disease dementia, and multiple subcortical lacunar strokes causing dementia all have reasonable insight and clue well on memory tasks.

References:

Knopman DS, DeKosky ST, Cummings JL, et al. Practice parameter: diagnosis of dementia (an evidence-based review). Report of the Quality Standards Subcommittee of the American Academy of Neurology. Neurology 2001;56:1143-1153.

Question 63: Behavioral/Psychiatry - Neurobehavioral/Neuropsychological Exam

Discussion:

The amnesia of Transient Global Amnesia affects recall of recent events and impairs new learning (anterograde memory). There is often some retrograde memory loss but generally involving only recent events. Patients are usually disoriented as to date and location, probably because of their inability to build upon new memory. TGA spares immediate recall, remote memory, language and procedural memory (e.g. playing a musical instrument). Details of identity are also spared.

References:

Moore, DP and Puri, BK. Textbook of Clinical Neuropsychiatry and Behavioral Neuroscience.

Question 71: Behavioral/Psychiatry - Behavioral Complications of Systemic Disease

Discussion:

The patient presents with symptoms of mania including abnormally euphoric, grandiose mood, adverse effect on work or social interactions, as well as unusually high energy level.

Though a patient may present with a primary mood disorder anytime during life, her acute illness and treatment with medication makes this less likely especially in light of her lack of psychiatric history in the past. A stroke causing injury to the right ventral prefrontal cortex could cause acute mania but usually would cause other neurological symptoms on examination. A delirium usually causes fluctuations in consciousness and is less likely in a patient who is alert and oriented. Sun-downing is the exacerbation of confusion that occurs in patients with dementia as the day progresses. Though it can cause sleep disruption and psychomotor agitation, usually the patient is not oriented and confused.

Antibiotics such as macrolides, beta lactam, as well as quinolones have been implicated in cases of acute mania and psychosis and in regard to this patient is the most likely reason for her symptoms.

References:

Lambrichts S, Van Oudenhove L, Sienaert P. Antibiotics and mania: A systematic review. J Affect Disord. 2017 Sep; 219: 149-156..

Question 78: Behavioral/Psychiatry - General Psychiatry

Discussion:

Inabilty to recall important personal information, such as your name, is characteristic of an amnesia with a psychiatric cause, such as a dissociative fugue or dissociative identity disorder. While memory problems can be profound in organic amnestic disorders, personal identity is not typically lost.

References:

American Psychiatric Association. Diagnostic and statistical manual of mental disorders (DSM-5). 5th ed. Arlington, VA: American Psychiatric Association, 2013.

American Psychiatric Association. Diagnostic and statistical manual of mental disorders (DSM-5). 5th ed. Washington DC: American Psychiatric Publishing, 2013.

Sadock BJ, Sadock VA, Ruiz, P. Kaplan and Sadock's Synopsis of psychiatry: behavioral sciences/clinical psychiatry. 11th ed. Philadelphia: Lippincott, Williams & Wilkins, 2015.

Question 81: Behavioral/Psychiatry - General Psychiatry

Discussion:

The patient's symptoms are most consistent with post-traumatic stress disorder (PTSD). PTSD presents with a greater than one-month history of re-experiencing the initial trauma through re-living or nightmares, active and passive avoidance symptoms of environmental triggers that could replay the trauma, psychomotor arousal such as irritability or insomnia, and amnesia of the initial event that threatened the safety of the individual or a loved one.

Frontotemporal dementia is a neurodegenerative disease which can present with irritability and lack of empathy but does not have the other symptoms noted above. Her presentation and symptom duration are not consistent with malingering or an adjustment disorder (no longer than 6 months).

References:

Bryant, R. Post-traumatic stress disorder vs traumatic brain injury. Dialogues in Clinical Neurosciences 2011; 13:251-26

Question 87: Behavioral/Psychiatry - Neurobehavioral/Neuropsychological Exam

Discussion:

The Wisconsin Card Sort Test (WCST), which challenges a patient to change cognitive sets without warning, is particularly sensitive to frontal damage. Language skills may be unaffected, and vocabulary is often spared. Face recognition and visual perception abnormalities such as hemi-inattention syndromes are most often associated with damage to the parietal, temporal, or occipital lobes, rather than the frontal lobes. Therefore, the best answer is the WCST.

References:

Kimberg DY, D'Esposito M, Farah MJ. Frontal lobes: cognitive neuropsychological aspects. In: Feinberg TE, Farah MJ, editors. Behavioral neurology and neuropsychology. New York: McGraw-Hill, 1997.

Question 91: Behavioral/Psychiatry - Behavioral Complications of Systemic Disease

Discussion:

Toluene toxicity is often the result of "recreational" abuse by sniffing and inhaling fumes from spray paint cans. Patients who chronically inhale toluene vapors develop dementia (clinically consistent with subcortical dementia), cerebellar ataxia and long tract findings, and in some cases cranial nerve palsies. It is not uncommon for these patients to also manifest a paranoid psychosis. MRI demonstrates a diffuse leukoencephalopathy, cerebral atrophy, and T2 hypointense lesions of the thalamus and/or the basal ganglia.

References:

Filley CM. The behavioral neurology of white matter. New York: Oxford University Press, 2001.

Question 94: Behavioral/Psychiatry - Dementia

Discussion:

Patients with posterior cortical atrophy present with progressive deficits that affect the dorsal and ventral streams of vision. They tend to have preserved insight and lack the characteristic memory deficits which are pathognomonic for Alzheimer disease. The angular gyrus syndrome results from an infarct or mass lesion affecting the angular gyrus on the dominant side. The syndrome consists of difficulty with naming, reading, writing, memory and contains the elements of a Gerstmann syndrome. Patients with semantic dementia lose conceptual knowledge of memories and words. They tend to have frequent pauses in their speech and can present with prosopagnosia.

References:

McMonagle P, Deering F, Berliner Y, Kertesz A. The cognitive profile of posterior cortical atrophy. Neurology 2006;66:331-338.

Question 98: Behavioral/Psychiatry - Language Disorders

Discussion:

Semantic dementia is a subtype of frontotemporal lobar degeneration. Patients early on have fluent spontaneous speech but have simplified content and anomic substitutions with general words. They also fail to correctly read or spell irregular words. As a variant of frontotemporal dementia, social inappropriateness and intrusive behaviors as well as depression is common.

Patients with corticobasal degeneration and primary progressive aphasia usually present with a nonfluent aphasia. Posterior cortical atrophy usually presents with visuospatial and visuoperceptual abnormalities. Alzheimer dementia's language issues are usually word-finding difficulties as well as memory and language retrieval abnormalities.

References:

Kertesz A. Frontotemporal dementia: a topical review. Cogn Behav Neurol 2008;21:127-133.

van der Zee J, Sleegers K, Van Brockhoven C. Invited article: the Alzheimer disease-frontotemporal lobar degeneration spectrum. Neurology 2008;71:1191-1197.

Question 103: Behavioral/Psychiatry - Genes, Biomarkers, & Networks

Discussion:

This patient is presenting with a history that is suggestive of multiple system atrophy (MSA). This condition can manifest with parkinsonism, cerebellar dysfunction, or pyramidal tract signs. Most patients will invariably manifest some symptoms of autonomic dysfunction. Patients with MSA frequently have alpha-synuclein inclusions distributed throughout the cortex.

References:

Possin KL, Kaufer DI. Parkinsonian dementias. Continuum Lifelong Learning Neurol 2010;16:57-79.

Question 106: Behavioral/Psychiatry - Anatomic syndromes

Discussion:

Contusion of the orbitofrontal cortex is associated with social disinhibition. Apathy, depression and loss of task set is more commonly seen in dorsolateral prefrontal lesions. Akinetic mutism is more commonly associated with medial frontal lesions.

References:

moore. Neuropsychiatry and behavioral neuroscience. New York: Oxford University Press, 2003.

Question 114: Behavioral/Psychiatry - Anatomic syndromes

Discussion:

Anton syndrome, (the denial of blindness), despite objective evidence of visual loss, is typically associated with bilateral posterior cerebral artery territory infarction producing cortical blindness plus memory impairment.

References:

Moore. Neuropsychiatry and behavioral neuroscience. New York: Oxford University Press, 2003.

Question 118: Behavioral/Psychiatry - General Psychiatry

Discussion:

This woman has had her first bout of major depression. She received successful treatment with an antidepressant after 2 months (acute phase). Effective treatment with antidepressants should be continued for at least 4 to 9 months more (continuation phase) before she is reevaluated for a potential medication taper.

References:

American Psychiatric Association. Practice guideline for the treatment of patients with major depressive disorder. 2nd ed. Am J Psychiatry 2000;157(Suppl 4):1-45.

American Psychiatric Association. PRACTICE GUIDELINE FOR THE Treatment of Patients With Major Depressive Disorder Third Edition (2010). https://psychiatryonline.org/pb/assets/raw/sitewide/practice_guidelines/guidelines/mdd.pdf

Question 129: Behavioral/Psychiatry - Dementia

Discussion:

Tetrabenazine is a reversible depletor of monoamines (dopamine, norepinephrine, epinephrine, serotonin, others). It reduces the uptake of dopamine and other monoamines into synaptic vesicles and blocks their transport. Because it provides greater selectivity for dopamine than the other monoamines, it particularly reduces dopaminergic activity in the brain.
 Haloperidol, perphenazine, and trifluoperazine are antipsychotics with a mechanism of action of antagonism of dopamine receptors in the mesolimbic and mesofrontal systems. They block postsynaptic mesolimbic dopaminergic D1 and D2 receptors in the brain. Lorazepam and other benzodiazepines may act by enhancing the effects of GABA in the brain.

References:

Huntington Study Group. Tetrabenazine as antichorea therapy in Huntington disease: A randomized controlled trial. Neurology 2006;66:366-372

Question 138: Behavioral/Psychiatry - Behavioral Complications of Systemic Disease

Discussion:

This is the history of a young man with AIDS. He subacutely developed progressive multifocal leukoencephalopathy (PML), a JC papovavirus that affects immunocompromised patients. It has a predilection for the white matter in the bilateral occipito-parietal regions. This is seen on T2 images of an MRI as large hyperintense white matter lesions in the occipitoparietal regions. Visual agnosia and Balint syndrome are some of the clinical manifestations of the disease.

References:

Brew BJ, Davies NW, Cinque P, et al. Progressive multifocal leukoencephalopathy and other forms of JC virus disease. Nat Rev Neurol 2010;6(12):667-679.

Question 142: Behavioral/Psychiatry - Anatomic syndromes

Discussion:

Right-left confusion occurs with dominant parietal lobe lesions, and can be associated with finger agnosia, agraphia and acalculia, as well as alexia (Gerstmann syndrome). Neglect or denial of the contralateral (usually left) half of the body and space generally results from damage to the non-dominant parietal lobe. Occasionally, neglect can be seen in the contralateral body and space with a dominant parietal lobe injury, but that would most likely involve right body and space. Dressing apraxia appears to be a related phenomenon and has been seen in patients with lesions in the same area. Impaired ability to perceive emotions (alexithymia) is a personality dysfunction seen in some psychiatric conditions including affective disorders and autism, with unclear specific localization. Prosopagnosia results from occipital or occipitotemporal lesions, generally bilateral.

References:

Moore, DP and Puri, BK. Textbook of Clinical Neuropsychiatry and Behavioral Neuroscience.

Question 151: Behavioral/Psychiatry - General Psychiatry

Discussion:

Patients with factitious disorder often have comorbid borderline and antisocial personality disorders. Clues to borderline personality are the rapid switch from overvaluing her doctor to devaluing him (dichotomous thinking) and the multiple scars on her wrists.

References:

American Psychiatric Association. Diagnostic and statistical manual of mental disorders (DSM-5). 5th ed. Arlington, VA: American Psychiatric Association, 2013.

Sadock BJ, Sadock VA, Ruiz, P. Kaplan and Sadock's Synopsis of psychiatry: behavioral sciences/clinical psychiatry. 11th ed. Philadelphia: Lippincott, Williams & Wilkins, 2015.

Question 152: Behavioral/Psychiatry - Language Disorders

Discussion:

Wernicke aphasia is characterized by impairments in comprehension, repetition, reading, writing, and naming, with fluent semantically paraphasic speech. Phonemic errors are more typical of Broca's aphasia, loosening of associations may mimic the rambling jargon of Wernicke aphasia, but can be distinguished by intact comprehension.

References:

Moore, DP and Puri, BK. Textbook of Clinical Neuropsychiatry and Behavioral Neuroscience.

Question 155: Behavioral/Psychiatry - Genes, Biomarkers, & Networks

Discussion:

The patient?s presentation is most concerning for Creutzfeldt-Jakob Disease (CJD). CSF studies would be important to rule in vs. rule out CJD. Detectable 14-3-3 protein in CSF is indicative of substantial, relatively rapid neuronal destruction seen in CJD; other rapidly progressive dementias; vascular, inflammatory, neoplastic, and metabolic CNS disorders. NSE, like 14-3-3, is elevated in any condition in which there is rapid neuronal death including CJD and hypoxic injury. Amyloid protein is decreased in Alzheimer disease but has no role in CJD evaluation. Tau is increased in Alzheimer disease but is several fold more so in CJD. Real-time quaking-induced conversion (RT-QuIC) is a method to detect prion-seeding activity in CSF samples. Patient CSF is added to wild-type prion protein and a positive signal is obtained if patient CSF contains infectious prion protein and is able to convert the wild-type protein to infectious forms. RT-QuIC sensitivity is 96% and specificity is 100%.

References:

Zanusso G, Monaco S, Pocchiari M, Caughey B.. Advanced tests for early and accurate diagnosis of Creutzfeldt-Jakob disease.. Nat Rev Neurol 2016;12(6):325-33.

Sanchez-Juan P, Green A, Ladogana A, Cuadrado-Corrales N, S‡chez-Valle R, Mitrov¥E, Stoeck K, Sklaviadis T, Kulczycki J, Hess K, Bodemer M, Slivarichov ¦, Saiz A, Calero M, Ingrosso L, Knight R,. CSF tests in the differential diagnosis of Creutzfeldt-Jakob disease.. Neurology 2006;67(4):637-43.

Matilde Bongianni, PhD; Christina Orr, PhD; Bradley R. Groveman, PhD; Luca Sacchetto, MD; Michele Fiorini, PhD; Giovanni Tonoli, MD; Giorgio Triva, BS; Stefano Capaldi, PhD; Silvia Testi, PhD; Sergio. Diagnosis of Human Prion Disease Using Real-Time Quaking-Induced Conversion Testing of Olfactory Mucosa and Cerebrospinal Fluid Samples. JAMA Neurol. 2017;74(2):155-162.

Question 157: Behavioral/Psychiatry - Neurobehavioral/Neuropsychological Exam

Discussion:

Spelling "WORLD" backward or alternatively doing serial 7s is the assessment for attention and concentration. Other components of the MMSE listed as choices test language (naming, reading comprehension), construction and short-term memory.

References:

Kaufer, Daniel I.. Neurobehavioral Assessment. Continuum Lifelong Learning in Neurology - Behavioral Neurology and Neuropsychiatry 2015; vol. 21 (3): 600-604

Question 163: Behavioral/Psychiatry - Language Disorders

Discussion:

Primary progressive aphasia (PPA) is a neurodegenerative process that affects language. Three variants of PPA have been described; semantic dementia, nonfluent/agrammatic aphasia and logopenic aphasia. Patients with logopenic aphasia have significant atrophy in the left posterior parasylvian or parietal region, whereas patients with semantic dementia have atrophy in the left anterior temporal regions and patients with nonfluent/agrammatic aphasia have atrophy involving the left frontoinsular region. Atrophy of the left medial temporal region is associated with Alzheimer’s disease. Atrophy in the orbitofrontal region is associated with behavior variant frontotemporal dementia.

References:

Gorno-Tempini, M.L., Hillis, A.E., Weintraub, S., Kertesz, A., Mendez, M., Cappa, S.F., Ogar, J.M., Rohrer, J.D., Black, S., Boeve, B.F., Manes, F., Dronkers, N.F., Vandenberghe, R.et. al. Classification of Primary Progressive Aphasia and its variants.. Neurology; 2011; 76: 1006-1014.

Question 164: Behavioral/Psychiatry - Psychopharmacology

Discussion:

Valproate is the only medication listed which has been shown to be effective as a mood stabilizer and to treat the symptoms of mania in patients with bipolar disorder. The other medications listed have not been proven effective in the treatment of patients with bipolar disorder.

References:

Dobovsky, Steven L.. Mania. Continuum Lifelong Learning in Neurology - Behavioral Neurology and Neurosychiatry 2015; vol. 21 (3); 747 -751

Question 175: Behavioral/Psychiatry - Neurobehavioral/Neuropsychological Exam

Discussion:

Balint syndrome, identified by Rezs (Rudolf) Bàlint in 1909, is characterized by optic ataxia (the inability to accurately reach for objects), optic apraxia (the inability to voluntarily guide eye movements/ change to a new location of visual fixation), and simultanagnosia (the inability to perceive more than one object at a time, even when in the same place). Balint syndrome is the result of visual binding deficits. Balint syndrome has been found in patients with bilateral damage to the posterior parietal cortex (and rarely, the frontal lobe; perhaps due to parietal frontal eye-field disconnection). The primary cause of the damage and the syndrome can originate from multiple strokes, Alzheimer disease, or intercranial tumors. Balint Syndrome has been reported as a developmental defect in children (Gillen and Dutton, 2003).

References:

Cummings JL, Mega MS. Neuropsychiatry and behavioral neuroscience. New York: Oxford University Press, 2003.

Question 180: Behavioral/Psychiatry - Psychopharmacology

Discussion:

Serotonin syndrome is characterized by mental status changes, autonomic instability and neuromuscular hyperactivity. This syndrome may be caused by the combination of SSRIs with other drugs that inhibit the reuptake of serotonin as well as certain illicit drugs (including cocaine). Anticholinergic syndrome is caused by inhibition of the muscarinic cholinergic receptors and is characterized by dry skin. Neuroleptic malignant syndrome is caused by dopamine receptor blockade usually secondary to an adverse reaction to antipsychotic medications. It is characterized by muscle rigidity followed by hyperthermia and altered mental status. Malignant hyperthermia is a rare condition linked to mutations in the ryanodine receptor gene and exposure to anesthetic agents such as succinylcholine. It is characterized by muscle rigidity and hypermetabolic state. Toxic shock syndrome is a life-threatening illness generally caused by infection with Staphylococcus aureus. It is characterized by rash, hypotension, high fever and multiorgan failure.

References:

Saddock, B and Saddock, V.. Synopsis of Psychiatry Behavioral Sciences/Clinical Psychiatry Eleventh Edition. Psychopharmacologic Treatment. In: Grebb, JA, Pataki, CS, Sussman, N editors. Philadelphia, PA:Lippincott Williams & Wilkins, 2007: 923-929.

Question 182: Behavioral/Psychiatry - Developmental Disorders

Discussion:

A toddler with classic Rett syndrome appears normal to her parents for most of the first year of life except for possible mild motor delays. Sometime between 1 and 2 years, the toddler experiences a regression of these skills. She stops playing with toys, stops responding to the spoken word, and stops using the few single words she has learned. She becomes withdrawn and loses interest in social interaction and stops walking. Purposeful hand use is replaced by stereotypic hand movements. The lost developmental skills are never recovered; and she moves through life at a level of profound intellectual disability often accompanied by seizures. MeCP2 gene mutation is the cause of Rett syndrome.

Aspartoacylase deficiency is the cause of Canavan disease which typically appears in early infancy and progresses rapidly from that stage with abnormal muscle tone, poor head control, and megalocephaly. Neonatal hypoxic ischemic injury is the cause of cerebral palsy, a permanent movement disorder with or without mental dysfunction. EpM2A gene mutation is the cause of Lafora body disease with symptoms of seizures, drop attacks, myoclonus, and ataxia manifesting in children from 10 to 17 years old. Copper accumulation is the cause of Wilson's disease, with symptoms typically beginning between 5 and 35 years old and manifesting with behavioral changes, tremors, hallucinations, and liver dysfunction from copper overload.

References:

Menkes JH, Sarnat HB. Textbook of child neurology. 6th ed. Philadelphia: Lippincott, Williams & Wilkins, 2000.

Question 183: Behavioral/Psychiatry - Behavioral Complications of Systemic Disease

Discussion:

Hashimoto's Thyroiditis, identified by antithyroid antibodies, can cause cognitive dysfunction including confusion, memory loss, aphasia and word finding problems and seizures. Hints include the high dose of thyroid medication with the thyroid-stimulating hormone still elevated. Evidence of nonspecific inflammatory markers such as polyclonal gammopathy may be present. Vitamin B12 deficiency may be associated with anemia but does not typically cause seizures. Homocysteine and methylmalonic acid may be elevated in vitamin B12 deficiency. Vasculitis and seizures due to lupus are often accompanied by new infarcts.

References:

Chaves P. de Holanda, N, Dantas de Lima, D, Cavalcanti, t, Lucena, C and Bandeira, F. Hashimoto's Encephalopathy: Systemic Review of the Literature and an Additional Case. J. of Neuropsychiatry 2011; 23; 384-390

Slatosky J, Shipton B, Wahba H. Thyroiditis: differential diagnosis and management. Am Fam Physician 2000;61:1047-1052, 1054.

Question 186: Behavioral/Psychiatry - Behavioral Complications of Systemic Disease

Discussion:

Patients with REM behavior disorder lack the usual limb paralysis that normally accompanies REM sleep. Therefore, they act out their dreams, which can often involve aggressive or violent behavior. Non-REM sleep disorders such as somnambulism do not usually involve violent behaviors, although they can in rare cases. Frontal lobe seizures rarely lead to complex violent behavior. Post-traumatic stress disorder can lead nightmares which do not usually lead to violence during sleep.

References:

American Psychiatric Association. Diagnostic and statistical manual of mental disorders (DSM-5). 5th ed. Washington DC: American Psychiatric Publishing, 2013.

Moore. Neuropsychiatry and behavioral neuroscience. New York: Oxford University Press, 2003.

Question 301: Behavioral/Psychiatry - General Psychiatry

Discussion:

Opioid intoxication causes pupillary constriction. Alcohol withdrawal, cocaine intoxication, hallucinogen intoxication, and amphetamine intoxication causes pupillary dilation.

References:

Sadock BJ, Sadock VA. Kaplan & Sadock's Pocket handbook of clinical psychiatry. 5th ed. Philadelphia: Lippincott, Williams & Wilkins, 2010.

Question 311: Behavioral/Psychiatry - Developmental Disorders

Discussion:

Up to 40% of patients with Tourette syndrome have obsessive-compulsive disorder (OCD) and first-degree relatives of Tourette patients also have a higher risk for the development of OCD. The other choices occur at a frequency similar to the general population.

References:

Sadock BJ, Sadock VA, Ruiz, P. Kaplan and Sadock's Synopsis of psychiatry: behavioral sciences/clinical psychiatry. 11th ed. Philadelphia: Lippincott, Williams & Wilkins, 2015.

Question 317: Behavioral/Psychiatry - General Psychiatry

Discussion:

Catatonia may be seen in a number of medical, neurological, and psychiatric conditions. Of the psychiatric causes, bipolar disorder is most common. Patients may present with a host of clinical features including akinetic mutism, catalepsy, waxy flexibility, echopraxia and echolalia, utilization behavior, and despite extreme negativism, may manifest automatic obedient behavior. When the patient is severely impaired, ECT is a treatment of choice. Benzodiazepines, such as lorazepam, also may be beneficial.

References:

Moore. Neuropsychiatry and behavioral neuroscience. New York: Oxford University Press, 2003.

Question 321: Behavioral/Psychiatry - Genes, Biomarkers, & Networks

Discussion:

The 14-3-3 protein is elevated in prion disorders, in contrast to most other dementing disorders. The protein elevation reflects neuronal destruction and so can be elevated in any disease that results in rapid neuronal death, such as trauma, stroke, or encephalitis. Classic findings of prion disorders include hyperekplexia (exaggerated startle), insomnia, encephalopathy, and ataxia.

References:

Bradley WG, Daroff RB, Fenichel GM, et al, editors. Neurology in clinical practice. 3rd ed. New York: Butterworth-Heinemann, 1999.

Question 323: Behavioral/Psychiatry - Dementia

Discussion:

An asymmetric rigid parkinsonism manifested by focal dystonia and apraxia are classic early features seen in most patients with corticobasal syndrome. The presence of an alien limb while almost diagnostic is not universally present.

References:

Moore. Neuropsychiatry and behavioral neuroscience. New York: Oxford University Press, 2003.

Question 328: Behavioral/Psychiatry - General Psychiatry

Discussion:

DSM-5 has reframed the dementia nomenclature in terms of mild and major neurocognitive disorder (NCD). The new schema focuses on a spectrum of functioning such that symptoms range from does not interfere with functioning or independence (Mild) to interferes to the point of needing assistance (Major). In each classification, cognitive decline can occur in one or more areas: learning and memory, language, executive functioning, complex attention, perceptual-motor, social cognition. Age of onset and duration of symptoms do not factor into the distinction between mild and major NCD. Etiology of symptoms is specified as a subtype of NCD such as traumatic brain injury or Alzheimer disease.

References:

American Psychiatric Association. Diagnostic and statistical manual of mental disorders (DSM-5). 5th ed. Arlington, VA: American Psychiatric Association, 2013.

Joseph R. Simpson. DSM-5 and Neurocognitive Disorders. Journal of the American Academy of Psychiatry and the Law Online 2014;42(2):159-164

Question 330: Behavioral/Psychiatry - Anatomic syndromes

Discussion:

The locked-in syndrome is characterized by being mute, quadriplegic, with preserved consciousness demonstrated by blinking or voluntary vertical eye movements with inability to voluntarily move eyes horizontally. Rarely there may be complete paralysis of the eyes as well. The locked-in syndrome is not coma; it results from lesions below the mid pons that preserves the brainstem reticular activating system for arousal and the brain for consciousness. Locked-in syndrome usually has preserved pupil reactivity and hearing as well.

References:

Posner JB, Saper CB, Schiff ND, Plum F. Plum and Posner's diagnosis of stupor and coma. 4th ed. New York: Oxford University Press, 2007.

Question 335: Behavioral/Psychiatry - Neurobehavioral/Neuropsychological Exam

Discussion:

A right parietal lobe tumor could interfere with the optic radiations and cause a left inferior quadrantanopsia (spares Meyer loop). This tumor could cause impaired graphesthesia in the left hand only, not both. Gerstmann syndrome may occur if the left (dominant) parietal lobe was affected. Receptive aprosody may occur in right temporoparietal lesions. Neglect is a common finding in right parietal lesions.

References:

Weintraub S, Mesulam MM. Right cerebral dominance in spatial attention. Arch Neurol 1987;44:621-625.

Question 344: Behavioral/Psychiatry - Psychopharmacology

Discussion:

Excess dopamine is often attributed in psychosis and increased novelty seeking. Acetylcholine is associated with memory. Substance P is linked to control of pain. Excessive norepinephrine is associated with reward dependency and vigilance. Low serotonin is associated with depression.

References:

Menza MA, Golve LI, Cody RA, Forman NE. Dopamine-related personality traits in Parkinson's disease. Neurology 1993;43:505-508.

Question 347: Behavioral/Psychiatry - Neurobehavioral/Neuropsychological Exam

Discussion:

HIV infection can result in minor cognitive and motor disorder, HIV-associated mild neurocognitive disorder, and HIV-associated dementia. The earliest symptoms revolve around mental slowing and processing speed. Tests that assess processing speed, including Trails A and B, grooved pegboard, Symbol Digit Modalities Test, and the HIV Dementia Scale are likely to be abnormal early in the disease course.

References:

Mesulam MM. Primary Progressive aphasia.. Ann Neurol 2001; 49 (4): 425-432

Question 354: Behavioral/Psychiatry - Psychopharmacology

Discussion:

Dextromethorphan (combined with quinidine which serves to increase the bioavailability of dextromethorphan) is a dual action glutamate inhibitor, via sigma-1 agonist activity and also via NMDA receptor antagonism; these actions are believed to help regulate excitatory neurotransmission to diminish the unpredictable emotional episodes of pseudobulbar affect. Sigma-1 receptors are expressed in specific regions of the brain such as layers of the cortex, hippocampus, hypothalamic nuclei, substantia nigra and Purkinje cells in the cerebellum. Although the exact molecular action of sigma-1 receptors is still unclear, a number of studies have demonstrated that they play a role as a modulator of ion channels (K+ channels; N-methyl-D-aspartate receptors [NMDA]; inositol 1,3,5 trisphosphate receptors). Sigma-1 agonists, while having no effects by themselves, cause the amplification of signal transductions incurred upon the stimulation of the glutamatergic, dopaminergic, IP3-related metabotropic, or nerve growth factor-related systems. Thus, it is hypothesized that sigma-1 receptors, at least in part, are intracellular amplifiers creating a super sensitized state for signal transduction in the biological system.

References:

Su TP, Hayashi T. Understanding the molecular mechanism of sigma-1 receptors: towards a hypothesis that sigma-1 receptors are intracellular amplifiers for signal transduction. Curr Med Chem 2003;10(20):2073-2080.

Question 367: Behavioral/Psychiatry - Anatomic syndromes

Discussion:

Lesions of the dorsomedial nucleus (commonly seen in Korsakoff syndrome) result in encoding deficits and therefore memory loss. Lesions of the paramedian region of the thalamus generally result in apathy, disinterest and lack of drive. Lesions of the ventral posterior region generally result in sensory loss. Lesions of the intralaminar and reticular nuclei affect normal alertness.

References:

Brazis, P, Masdeu, J and Biller, J. The Anatomic Localization of Lesions in the Thalamus In: Localization in Clinical Neurology. Boston: Little Brown and Company, 1996; 401-425.

Question 368: Behavioral/Psychiatry - Psychopharmacology

Discussion:

Bupropion has had a low incidence of erectile dysfunction associated with its use. All of the selective serotonin reuptake inhibitors (SSRIs) and SNRIs have been reported to have erectile dysfunction as a side effect. Amitriptyline also causes erectile dysfunction.

References:

Arana GW, Rosenbaum JF. Handbook of psychiatric drug therapy. 5th ed. Philadelphia: Lippincott, Williams & Wilkins, 2005.

Question 380: Behavioral/Psychiatry - Dementia

Discussion:

The clinical criteria for frontotemporal dementia (FTD) include gradual onset with progressive decline, changes in personal hygiene, loss of social decorum, lack of insight, emotional blunting, and loss of empathy. FTD has been linked to motor neuron disease, as well as parkinsonism, both in the patients with FTD as well as in family members.

References:

Strong MJ, Lomen-Hoerth C, Caselli RJ, et al. Cognitive impairment, frontotemporal dementia, and the motor neuron diseases. Ann Neurol 2003;54:S20-23.

Question 385: Behavioral/Psychiatry - Psychopharmacology

Discussion:

Atypical antipsychotics have been reported to cause increased triglycerides, diabetes, weight gain, ischemic cerebral vascular events and increased irritability. Of these, the most commonly reported adverse event is hyperglycemia and weight gain.

References:

Zheng L, Mack WJ, Dagerman KS, Hsiao JK, et al.. Metabolic changes associated with second-generation antipsychotic use in Alzheimer's disease patients: the CATIE-AD study.. Am J Psychiatry 2009;166:583-590

Atmaca M, Kuloglu M, Tezcan E, Ustundag B. Serum leptin and triglyceride levels in patients on treatment with atypical antipsychotics. J Clin Psychiatry 2003;64:598-604.

Question 388: Behavioral/Psychiatry - Genes, Biomarkers, & Networks

Discussion:

TAR DNA-binding protein 43 (TDP-43) is a major protein component of the ubiquitin-immunoreactive inclusions characteristic of sporadic and familial frontotemporal lobar degeneration with ubiquitin-positive, tau-negative inclusions (FTLD-U), with and without motor neuron disease, as well as in sporadic amyotrophic lateral sclerosis (ALS). These conditions with TDP-43 do not have tau, beta-amyloid, or alpha-synuclein inclusions. Tau inclusions are seen in some other types of frontotemporal dementias and Alzheimer disease. Beta-amyloid inclusions are classically seen in Alzheimer disease. Alpha-synuclein inclusions are seen in dementia with Lewy bodies and Parkinson disease. Pick bodies are aggregations of tau protein in neurons associated with Pick disease, a subtype of frontotemporal lobar degeneration.

References:

Cairns NJ, Neumann M, Bigio EH, et al. TDP-43 in familial and sporadic frontotemporal lobar degeneration with ubiquitin inclusions. Am J Pathol 2007;171(1):227-240.

Neumann M, Sampathu DM, Kwong LK, et al. Ubiquitinated TDP-43 in frontotemporal lobar degeneration and amyotrophic lateral sclerosis. Science 2006;314(5796):130-133.

Question 395: Behavioral/Psychiatry - General Psychiatry

Discussion:

The patient is a severely depressed widowed male which places him at a higher risk for suicide. Vague suicidal statements such as talk of death or "joining" a deceased individual should always prompt further investigation to ascertain intent and degree of risk.

References:

Sadock BJ, Sadock VA, Ruiz, P. Kaplan and Sadock's Synopsis of psychiatry: behavioral sciences/clinical psychiatry. 11th ed. Philadelphia: Lippincott, Williams & Wilkins, 2015.

Clinical Adult

Question 9: Clinical Adult - Neurology of Systemic Disease

Discussion:

Midodrine is a prodrug that is metabolized in the liver to desglymidodrine, a potent alpha-1 adrenergic agonist that produces arterial and venous vasoconstriction. Unlike other sympathomimetics, midodrine has a predictable absorption and plasma half-life. It is currently the drug of second choice after fludrocortisone for management of neurogenic orthostatic hypotension. The dose is 10-40 mg/day. It should not be administered in the evening given the risk of supine hypertension. Scalp pruritus is a common side effect.

References:

Arnold A, Raj S.. Orthostatic Hypotension: A Practical Approach to Investigation and Management. Can J Cardiol. 2017 Dec;33(12):1725-1728

Gibbons C, Schmidt P, Biaggioni I, Frazier-Mills C et al.. The recommendations of a consensus panel for the screening, diagnosis, and treatment of neurogenic orthostatic hypotension and associated supine hypertension. J Neurol. 2017 Aug;264(8):1567-1582

Biaggioni I. Treatment: special conditions Orthostatic hypotension. Journal of the American Society of Hypertension 2015;9(1):67-69.

Question 10: Clinical Adult - Neuro-ophthalmology/Neuro-otology

Discussion:

Epilepsy related visual hallucinations are characteristically very brief and simple. They tend to occur in a hemifield and are associated with a description of motion. In this instance, ocular examination is normal making increased intracranial pressure and vitreous deposits unlikely. Medication-induced hallucinations may be unformed at times but would not generally be restricted to a hemifield. Migraine aura may be confounded with occipital seizures but is typically much longer lasting and classically consist of geometric patterns such as black and white zigzag lines which are often scintillating in character.

References:

Pelak VS. Visual Hallucinations and Higher Cortical Visual Dysfunction. Continuum 2009; vol 15 (4) : 94-96 Visual Hallucinations and Higher Cortical Visual Dysfunction.. Continuum 2009; vol 15 (4): 94-96.

Question 13: Clinical Adult - Cerebrovascular Disease

Discussion:

Acute ischemic stroke in the distribution of the anterior inferior cerebellar artery (AICA) is the leading cause of acute audiovestibular loss. Isolated hearing loss without other neurologic symptoms is associated with a labyrinthine artery infarction.

References:

Kim H, Lee H. Recent Advances in Understanding Audiovestibular Loss of a Vascular Cause. J Stroke. 2017 Jan; 19(1): 61?66.

Question 17: Clinical Adult - Critical Care/Stroke

Discussion:

In patients with status epilepticus intubation and general anesthesia can interfere with the observation of further seizure activity. In the absence of an EEG, pupillary dilatation and hypertension can be signs of persistent electrographic seizure activity. Hypotension, poikilothermia and hypoventilation are likely secondary to sedative and anesthetic agents. The elevation of serum creatine kinase suggests rhabdomyolysis secondary to prolonged convulsive activity and may persist for some time after seizures have ceased. Upgoing toes in this setting are a nonspecific finding and are consistent with persistent seizure activity, a postictal state, or a metabolic, toxic, or drug induced encephalopathy.

References:

Hocker SE. Status epilepticus. Continuum (Minneap Minn) 2015;21:1362-1383.

Bleck TP. Status epilepticus and the use of continuous EEG monitoring in the intensive care unit. Continuum Lifelong Learning Neurol 2012;18(3):560-578.

Question 19: Clinical Adult - Neuromuscular Disorders

Discussion:

Inclusion body myositis is an inflammatory condition in older individuals (male predominant) which is slowly progressive. Clinical features of early weakness and atrophy of select muscles is found: quadriceps, flexors of the forearms and ankle dorsiflexors. There are other associated laboratory and muscle biopsy findings. Motor neuron disease would be unlikely to run such a slowly progressive course and would be associated with other exam abnormalities (reflex changes, etc.); polymyositis is generally more fulminant, painful and symmetric; central core disease is congenital with fairly mild progression over life; both types of myotonic dystrophy are autosomal dominant, typically present earlier in life and have many systemic manifestations.

References:

Amato AA, Greenberg SA.. Inflammatory Myopathies. Continuum: Lifelong Learning in Neurology, 2013;19 (6):1615-1633.

Question 22: Clinical Adult - Epilepsy

Discussion:

This patient has focal epilepsy that appears to arise from her left medial temporal lobe. Long-term video EEG monitoring is necessary to confirm the seizure focus and for presurgical evaluation. Because the patient has failed polytherapy, adding a third agent is unlikely to achieve control of her epilepsy.

References:

Christopher T Skidmore. Adult Focal Epilepsies. Continuum 2016;22(1):94-115.

Question 26: Clinical Adult - Infectious Disease

Discussion:

This patient has a syndrome of recurrent, self-limiting, aseptic meningitis – which has also been called Mollaret meningitis. This syndrome is caused by the herpes simplex virus 2 and may benefit from treatment with acyclovir.

References:

Richard Whitley,MD. Herpes Simplex Virus Infections of the Central Nervous System. Continuum 2015;21(6):1704-1713.

Question 27: Clinical Adult - Movement Disorders

Discussion:

Huntington disease is an autosomal dominant movement disorder characterized by chorea, dementia and behavioral disturbances. The pathologic hallmark of Huntington disease is atrophy of the caudate and this can be visualized with an MRI of the head.

References:

Poston KL. Overview of rare movement disorders. Continuum Lifelong Learning Neurol 2010;16(1):56-69.

Jankovic JJ, Tolosa E. Parkinson's disease and movement disorders. 4th ed. Philadelphia: Lippincott, Williams and Wilkins, 2002.

Question 28: Clinical Adult - Motor Neuron/Nerve

Discussion:

This patient most likely has motor neuron disease, characterized by a mixture of upper and lower motor neuron signs in all four limbs. Cervical spinal stenosis could also produce painless four-limb weakness with upper motor neuron signs in the legs. Fasciculations and wasting in the lower extremities are not symptoms of cervical stenosis as they imply a disorder of the lower motor neuron at the lumbosacral level. Although patients with cervical stenosis may have spine and radicular pain, this is not always the case, and the absence of pain does not exclude cervical stenosis as a diagnosis.

References:

GOUTMAN, STEPHEN A. MD, MS. Diagnosis and Clinical Management of Amyotrophic Lateral Sclerosis and Other Motor Neuron Disorders. Continuum 2017;23(5):1332-1359

Question 30: Clinical Adult - Sleep

Discussion:

While managing a patient with obstructive sleep apnea, current symptoms, especially daytime sleepiness, AHI, and co-morbid cardio/cerebrovascular, metabolic, and pulmonary disorders should be taken into consideration. As indicated by the AHI, he has moderate obstructive sleep apnea (OSA) and co-morbid poorly controlled hypertension with significant daytime sleepiness. Therefore, his OSA should be aggressively managed to decrease the daytime sleepiness, and possibly better control of the hypertension. Among the options listed, CPAP, if used appropriately, is 100 % effective and thus would be the best option. Surgery has a success rate of ~ 50% with a high relapse rate. A dental appliance is might be beneficial in mild obstructive sleep apnea. Weight loss should be encouraged in all sleep apnea patients with BMI > 25; however, it is not helpful by itself. Hypnotic use by itself in moderate to severe obstructive sleep apnea might worsen sleep apnea and thus is not the best option.

References:

Pack AI. Advances in sleep-disordered breathing. Am J Respir Crit Care Med 2006;173:7-15.

Chesson A, Ferber R, Fry J, et al. Practice parameters for the indications for polysomnography and related procedures. Sleep 1997;20:406.

Question 31: Clinical Adult - Neuro-ophthalmology/Neuro-otology

Discussion:

This patient's symptoms together with the presence of bilateral papilledema suggest increased intracranial pressure, likely due to idiopathic intracranial hypertension (IIH, pseudotumor cerebri). Imaging will be necessary to exclude a neoplasm, venous sinus thrombosis, or other structural CNS lesion causing elevated intracranial pressure. In addition to symptoms of headache, transient visual obscurations, diplopia, and visual loss, many patients with IIH also experience pulsatile tinnitus.

References:

Randhawa S, Van Stavern GP. Idiopathic intracranial hypertension (pseudotumor cerebri). Curr Opin Ophthalmol 2008;19(6):445-453.

Friedmann DI, Liu GT, Digre KB. Revised Diagnostic criteria for the pseudotumor cerebri syndrome in adults and children. Neurology 2013;81:1159?1165

Giuseffi V, Wall M, Siegel PZ, et al. Symptoms and disease associations in idiopathic intracranial hypertension (pseudotumor cerebri): A case-control study. Neurology 1991;41:239-244

Question 35: Clinical Adult - Neuromuscular Disorders

Discussion:

This patient's signs and symptoms of sensory loss to pinprick with preservation of vibratory sense and reflexes, is most consistent with a small fiber neuropathy. His symptoms are compatible with leprosy, which occurs due to Mycobacterium leprae, a neurotropic bacterium. This diagnosis is supported by the distribution of this patient's sensory loss, which includes his ears and nose, and the fact that he has emigrated from a country endemic for leprosy.

References:

Robinson-Papp, Jessica MD. Infectious neuropathies. Continuum 2012;18(1)126-138.

Ooi W, Srinivasan J. Leprosy and the peripheral nervous system: basic and clinical aspects. Muscle Nerve 2004;30:393-409.

Michael K. Hehir, II, MD; ; Eric L. Logigian, MD, FAAN;. Infectious Neuropathies, Continuum lifelong learning p. 1274-1292, 2014, Vol.20, No.5.

Question 38: Clinical Adult - Movement Disorders

Discussion:

Propofol has been reported to cause dystonic reactions. This patient most likely has a dystonic reaction caused by propofol. Dystonic reactions are characterized by intermittent spasmodic or sustained involuntary contractions of muscles in the face, neck, trunk, pelvis, and extremities. Treatment with an anticholinergic agent (benztropine or diphenhydramine) usually resolves the symptom within a matter of minutes.

References:

Sherer J et. al. Diphenhydramine for acute extrapyramidal symptoms after propofol administration. Pediatrics 2017;139 (2)

Jankovic JJ, Tolosa E. Parkinson's disease and movement disorders. 4th ed. Philadelphia: Lippincott, Williams and Wilkins, 2002.

Question 41: Clinical Adult - Epilepsy

Discussion:

This patient most likely has focal seizures resulting from a lesion of the temporal lobe. Mesial temporal sclerosis is the most common etiology in adults with this disorder although other structural lesions of the temporal lobe (i.e. glioma, vascular malformation) are other possibilities. The likelihood of a meningioma in a young man is very low. Migraine is usually not associated with gustatory hallucination and there are other worrisome neurologic symptoms that make primary psychiatric disease unlikely.

References:

Rudzinski, LA.; Shih, JJ. The Classification of Seizures and Epilepsy Syndromes. Continuum Lifelong Learning in Neurology: June 2010 - Volume 16 - Issue 3, Epilepsy - pp 15-35

Sadler RM. The syndrome of mesial temporal lobe epilepsy with hippocampal sclerosis: clinical features and differential diagnosis. Adv Neurol 2006;97:27-37.

Question 46: Clinical Adult - Critical Care/Stroke

Discussion:

This patient has a large left cerebellar stroke with neurologic deterioration over the last couple of hours. While medical therapy can be attempted as a temporizing measure, this patient will likely need a suboccipital craniectomy given the size of the stroke and the rapid deterioration over hours.

References:

Powers, William J., Colin P. Derdeyn, Josè Biller, Christopher S. Coffey, Brian L. Hoh, Edward C. Jauch, Karen C. Johnston, S. Claiborne Johnston, Alexander A. Khalessi, Chelsea S. Kidwell, James F.. 2015 American Heart Association/American Stroke Association Focused Update of the 2013 Guidelines for the Early Management of Patients With Acute Ischemic Stroke Regarding Endovascular Treatment..

Question 49: Clinical Adult - Headache

Discussion:

Temporal arteritis most commonly presents in an elderly population with a unilateral dull, achy headache, often with scalp tenderness. Blindness is a major complication. This patient's symptoms are most suggestive of temporal arteritis. An erythrocyte sedimentation rate (ESR) should be sent and reviewed while the patient is in the emergency room. Elevation of the ESR should lead to urgent steroid therapy to avoid irreversible visual loss, with a temporal artery biopsy to follow as soon as possible to provide histologic proof of the diagnosis.

References:

Falardeau J. Giant cell arteritis. Neurol Clin 2010 Aug;28(3):581-91

Buttgereit F, Dejaco C, Matteson EL, Dasgupta B. Polymyalgia Rheumatica and Giant Cell Arteritis: A Systematic Review.. JAMA. 2016 Jun 14;315(22):2442-58.

Question 52: Clinical Adult - Headache

Discussion:

The trigeminal autonomic cephalgias are a group of primary headache disorders characterized by short-lasting episodes of severe unilateral headaches that are associated with ipsilateral cranial autonomic symptoms. This patient has Short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing (SUNCT) syndrome, as well described by the name, is characterized by very brief attacks of periorbital pain with ipsilateral tearing and eye redness. The attacks of SUNCT syndrome

resemble those of cluster headaches but are primarily differentiated by the much briefer attack duration and greater frequency in SUNCT than cluster headache. SUNCT can also resemble V1 trigeminal neuralgia but the latter should not have the prominent autonomic features of SUNCT.

References:

Continuum Life long learning, Headache p. 1191-121, 2015, Vol.21, No.4.

Goadsby, PJ. Trigeminal Autonomic Cephalgias. Continuum Lifelong Learning in Neurology 2012;18(4):883-895

Question 58: Clinical Adult - Headache

Discussion:

Triptans are contraindicated in the presence of known coronary artery disease due to the risk of precipitating vasospasm and coronary ischemia.

References:

Rizzoli PB. Acute and Preventive Treatment of Migraine. Continuum Lifelong Learning in Neurology 2012;18(4):764-782

Dodick D, Lipton RB, Martin V, et al. Consensus statement: cardiovascular safety profile of triptans (5-HT agonists) in the acute treatment of migraine. Headache 2004;(5):414-425.

Question 77: Clinical Adult - Neuro-ophthalmology/Neuro-otology

Discussion:

This patient has an isolated trochlear nerve palsy. Microvascular ischemia in the setting of high blood pressure and diabetes is the most common cause of this condition.

References:

Brazis PW, Masdeu JC, Biller J. Localization in clinical neurology. 6th ed. Philadelphia: Lippincott, Williams & Wilkins, 2011.

Question 84: Clinical Adult - Headache

Discussion:

The patient described has cluster headache and is being considered for prophylaxis of this condition. Ergotamine is an abortive treatment. Atenolol has little CNS penetration and is not recommended for headache prophylaxis; imipramine is more appropriate for migraine prophylaxis. Verapamil, a calcium channel blocker, is currently the preferred agent for prophylaxis of cluster headaches during a cluster. Verapamil can be titrated off once the patient has been headache free for more than 2 weeks as there is no known prophylactic benefit between clusters.

References:

Dodlick. Headaches. Continuum 2015;21:4:939-1249

Goadsby, PJ. Trigeminal Autonomic Cephalgias. Continuum Lifelong Learning in Neurology 2012;18(4):883-895

Question 85: Clinical Adult - Demyelinating Disease

Discussion:

The newly released oral platform agent for relapsing-remitting multiple sclerosis, fingolimod, is a sphingosine 1-phosphate receptor inhibitor. It's putative mechanism of action in MS is sequestration of lymphocytes in lymph nodes.

References:

Greenberg BM, Khatri BO, Kramer JF. Current and emerging multiple sclerosis therapeutics. Continuum Lifelong Learning Neurol 2010;16(5):59-67.

Question 88: Clinical Adult - Headache

Discussion:

Pseudotumor cerebri is characterized by headaches, visual obscurations and papilledema. Several medications including isotretinoin and other vitamin A-containing compounds are associated with the development of pseudotumor.

References:

Friedman DI. Medication-induced intracranial hypertension in dermatology. Am J Clin Dermatol. 2005;6(1):29-37.

Wall M. Papilledema and idiopathic intracranial hypertension (pseudotumor cerebri). In: Noseworthy JH, editor. Neurologic therapeutics: principles and practice. New York: Martin Dunitz, 2003;1730-1742.

Question 96: Clinical Adult - Cerebrovascular Disease

Discussion:

The window for administering IV alteplase is within 4.5 hours of the patient's last known well time. In patients beyond the 4.5 hours window, thrombectomy should be a consideration. In patients within the 6-hour window with a head CT demonstrating an ASPECTS > 6, no additional imaging is needed beyond a CT angiogram demonstrating a large vessel occlusion. The patient should, therefore, be taken for thrombectomy as soon as possible.

References:

Powers, William J., Colin P. Derdeyn, Josè Biller, Christopher S. Coffey, Brian L. Hoh, Edward C. Jauch, Karen C. Johnston, S. Claiborne Johnston, Alexander A. Khalessi, Chelsea S. Kidwell, James F.. 2015 American Heart Association/American Stroke Association Focused Update of the 2013 Guidelines for the Early Management of Patients With Acute Ischemic Stroke Regarding Endovascular Treatment..

Question 100: Clinical Adult - Neuro-ophthalmology/Neuro-otology

Discussion:

"HINTS to diagnose stroke in the acute vestibular syndrome" include the presence of skew eye deviation (vertical ocular misalignment), nystagmus which changes direction on eccentric gaze, and the absence of vestibulo-ocular reflex tested by the bedside horizontal impulse test. A brainstem lesion is highly likely when the acute vestibular syndrome is associated with any of these findings. Skew eye deviation is the most sensitive, being even more sensitive than brain MRI for the diagnosis of acute brainstem stroke in the first 48 hours of symptom onset. Neither nausea or vomiting, nor hearing loss, distinguishes central from peripheral vertigo. Unidirectional horizontal nystagmus is more compatible with a peripheral vestibular lesion.

References:

Kattah JC, Talkad AV, Wang DZ, et al. HINTS to Diagnose Stroke in the Acute Vestibular Syndrome. Stroke.2009;40:1-7

Question 102: Clinical Adult - Neurology of Systemic Disease

Discussion:

This is a young patient with stroke meeting criteria for the diagnosis of antiphospholipid syndrome. Given her multiple miscarriages (thrombotic events) and new stroke, anticoagulation would be the treatment of choice. Warfarin is recommended to prevent further thrombotic events.

References:

Garcia D, Erkan D. Diagnosis and Management of the Antiphospholipid Syndrome. N Engl J Med 2018; 378:2010-2021

Kernan WN, Ovbiagele B, Black HR, Bravata DM, Chimowitz MI, Ezekowitz MD, Fang MC, Fisher M, Furie KL, Heck DV, Johnston SC, Kasner SE, Kittner SJ, Mitchell PH, Rich MW, Richardson D, Schwamm LH. Guidelines for the prevention of stroke in patients with stroke and transient ischemic attack: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. Stroke. 2014;45:2160-2236

Question 105: Clinical Adult - Movement Disorders

Discussion:

The diagnosis of probable multiple system atrophy can be made in a patient with symptoms of autonomic failure (typically beginning with bladder and erectile dysfunction, with prominent orthostasis on examination) and no response to levodopa.

References:

Christopher W. Hess, MD; ; Michael S. Okun, MD, FAAN;. Diagnosing Parkinson Disease, Movement Disorders p. 1047-1063, 2016, Vol.22, No.4.

Wiliams D, Litvan I.. Parkinsonian Syndromes. Continuum: Lifelong Learning in Neurology 2013;19(5):1189-1212.

Question 108: Clinical Adult - Demyelinating Disease

Discussion:

Fingolimod has been associated with macular edema in approximately 1% of treated patients. The macula is found in the center of the retina and is responsible for sharp, straight-ahead vision. Fluid buildup causes the macula to swell and thicken. Before switching treatment, the etiology of her visual distortion should be confirmed with a retinal examination by ophthalmology. Her vision change is less likely to be secondary to optic neuritis since she does not have pain with eye movements and does not have an afferent pupillary defect.

References:

Greenberg BM, Khatri BO, Kramer JF. Current and emerging multiple sclerosis therapeutics. Continuum Lifelong Learning Neurol 2010;16(5):59-67.

Afshar A, Fern○□ez J,Patel R.et,al. Cystoid Macular Edema associated with Fingolimod Use for Multiple Sclerosis. Jama Ophthalmology 2013;131 (1):103-107.

Question 115: Clinical Adult - Spinal and Root Disorders

Discussion:

Weakness of ankle dorsiflexion could localize to the deep peroneal (fibular) nerve, common peroneal (fibular nerve), sciatic nerve, lumbosacral plexus, or L5 nerve root. The involvement of ankle eversion eliminates the deep peroneal (fibular) nerve ankle eversion is innervated by the superficial peroneal (fibular) nerve. The involvement of ankle inversion eliminates the common peroneal (fibular) nerve since ankle inversion is innervated by the tibial nerve. The sparing of ankle plantarflexion argues against either the lumbosacral plexus or the sciatic nerve. In this context, L5 is the most likely localization.

References:

Preston DC, Shapiro BE. Electromyography and neuromuscular disorders: clinical-electrophysiologic correlations. 3nd ed. Philadelphia: Elsevier, 2012.

Question 125: Clinical Adult - Other Pain Syndromes

Discussion:

This patient's symptoms are most compatible with trigeminal neuralgia (tic douloureux). Most cases of trigeminal neuralgia are thought to be due to compression of the trigeminal nerve by a vascular loop. Imaging is indicated to exclude other, though less common, structural causes such as a meningioma, cerebellopontine angle neoplasm, and aneurysm. Multiple sclerosis can also be a cause of trigeminal neuralgia, but that is less likely in this patient due to her age and lack of other signs and symptoms. In the absence of long tract and cerebellar findings, stroke is extremely unlikely.

References:

Cruccu, G. Trigeminal Neuralgia. Continuum Lifelong Learning in Neurology: April 2017, volume 23, p 396?420

Love S, Coakham HB. Trigeminal neuralgia pathology and pathogenesis. Brain 2001;124:2347-2360.

Cheshire WP. Trigeminal neuralgia: diagnosis and treatment. Curr Neurol Neurosci Rep 2005;5(2):79-85.

Question 130: Clinical Adult - Cerebrovascular Disease

Discussion:

The medial striate artery (known as the recurrent artery of Heubner) is a branch of the anterior cerebral artery that supplies part of the caudate head. The caudate head is also supplied by branches of the middle cerebral artery. The pericallosal arteries are branches of the anterior cerebral artery that supply medial aspects of both hemispheres. The anterior choroidal artery supplies the posterior limb of the internal capsule, the medial globus pallidus, and the lateral geniculate body. The posterior choroidal artery supplies the lateral geniculate body, pulvinar, posterior thalamus, hippocampus, and parahippocampal gyrus. The artery of Percheron is a variant that supplies both thalami.

References:

Brazis PW, Masdeu JC, Biller J. Localization in clinical neurology. 6th ed. Philadelphia: Lippincott, Williams & Wilkins, 2011.

Question 132: Clinical Adult - Cerebrovascular Disease

Discussion:

According to the SAMMPRIS Study, best medical management with high dose statin, blood pressure control, and dual antiplatelet therapy with aspirin and clopidogrel for 3 months is the optimal treatment for patients with stroke from severe intracranial atherosclerosis and was shown to be more efficacious than mechanical interventions. The WASID study showed that antiplatelets had overall better outcomes than anticoagulation for patients with severe intracranial atherosclerosis.

References:

Chimowitz M, Lynn M, Howlett-Smith H, Stern B, Hertzberg V, Frankel M, Levine S, Chaturvedi S, Kasner, S, Benesch C, Sila C, Jovin T. Comparison of Warfarin and Aspirin for Symptomatic Intracranial Arterial Stenosis. N Engl J Med 2005; 352:1305-1316

Chimowitz M, Lynn M, Derdeyn C, Turan T, Fiorella D, Lane B, et al.. Stenting versus Aggressive Medical Therapy for Intracranial Arterial Stenosis. N Engl J Med 2011;365:993-1003.

Question 134: Clinical Adult - Infectious Disease

Discussion:

This patient has bacteremia with a mobile mass in the aortic valve, so his strokes are likely from endocarditis. Treatment should be geared toward the underlying cause which is an infection of the valve and should be with antibiotics. Patients with endocarditis are at increased risk of forming mycotic aneurysms. Therefore, starting antiplatelets and anticoagulation can place

them at risk of significant intracranial hemorrhage should there be aneurysmal rupture. If antibiotic treatment fails, surgical valve replacement may be necessary.

References:

Kernan WN, Ovbiagele B, Black HR, Bravata DM, Chimowitz MI, Ezekowitz MD, Fang MC, Fisher M, Furie KL, Heck DV, Johnston SC, Kasner SE, Kittner SJ, Mitchell PH, Rich MW, Richardson D, Schwamm LH. Guidelines for the prevention of stroke in patients with stroke and transient ischemic attack: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. Stroke. 2014;45:2160-2236

Question 140: Clinical Adult - Epilepsy

Discussion:

For adults presenting with a first unprovoked seizure, there is a 21 to 45% chance of developing a recurrent seizure in the first 2 years after the first event. Risk factors that are most strongly associated with an increased risk include history of a prior brain insult and EEG with epileptiform abnormalities. (Level A evidence)

References:

Krumholz A, Wiebe S, Gronseth GS.. Evidence-based guideline: management of an unprovoked first seizure in adults.. Neurology 2015;84:1705-1713

Pedley TA, Mendiratta A, Walczak TS. Seizures and epilepsy. In: Ebersole JS, Pedley TA, editors. Current practice of clinical electroencephalography. 3rd ed. Philadelphia: Lippincott, Williams & Wilkins, 2003.

Question 141: Clinical Adult - Critical Care/Stroke

Discussion:

Cerebral vasospasm is a serious complication of subarachnoid hemorrhage typically occurring between the 4th and 14th day after hemorrhage. It often presents with focal neurologic deficits and drowsiness.

References:

Bele S1, Proescholdt MA2, Hochreiter A3, Schuierer G4, Scheitzach J5, Wendl C6, Kieninger M7, Schneiker A8, Brndl E9, Sch P10, Schebesch KM11, Brawanski A12.. Continuous intra-arterial nimodipine infusion in patients with severe refractory cerebral vasospasm after aneurysmal subarachnoid hemorrhage: a feasibility study and outcome results.. Acta Neurochir (Wien). 2015 Dec;157(12):2041-50. doi: 10.1007/s00701-015-2597-z. Epub 2015 Oct 6.

Lawton M, Vates E. Subarachnoid Hemorrhage. N Engl J Med 2017;377:257-66.

Question 143: Clinical Adult - Spinal and Root Disorders

Discussion:

Diabetic lumbosacral radiculoplexus neuropathy presents with acute and severe proximal lower limb pain, followed by muscle weakness and atrophy. It is the most commonly observed in patients with well-controlled type 2 diabetes mellitus.

References:

Bril V. Neuromuscular Complications of Diabetes Mellitus. Continuum 2014:20(3):531-544.

Question 144: Clinical Adult - Neuro-oncology

Discussion:

This patient developed hypertension, a seizure, and cortical blindness that is consistent with a reversible posterior leukoencephalopathy while on bevacizumab. Bevacizumab is also associated with an increased incidence of stroke, intracranial hemorrhage, and optic neuropathy. The seizure, somnolence, and normal pupillary responses are most consistent with reversible posterior leukoencephalopathy.

References:

DeAngelis LM, Posner JB. Neurologic complications of cancer. 2nd ed. New York: Oxford University Press, 2009.

Question 146: Clinical Adult - Neuro-ophthalmology/Neuro-otology

Discussion:

The history is consistent with Mal de debarquement syndrome, described by patients usually as a feeling of motion, rocking or swaying when there is no physical motion. This can be persistent and is most often provoked by an ocean voyage. The syndrome is notable for typically lacking nausea, vomiting, vertigo or other common vestibular symptoms as well as an absence of hearing symptoms. Patients usually feel some relief by being in motion themselves, either by driving or going back out on the ocean, and they feel most symptomatic when they are sitting still.

References:

Saha KC, Fife TD.. Mal de debarquement: review and proposed diagnostic criteria.. Neurology Clinical Practice 2015;5(3): 209-215.

Question 147: Clinical Adult - Epilepsy

Discussion:

This patient's symptoms and EEG findings are most consistent with juvenile myoclonic epilepsy (JME). JME is a generalized epilepsy that typically presents during adolescence or early adulthood. Patients with JME typically describe a history of morning myoclonic jerks, and both the generalized seizures and the myoclonic jerks commonly are precipitated by sleep deprivation and alcohol.

References:

Glauser TA, Cnaan A, Shinnar S, Hirtz DG, Masur D, Clark PO, Capperelli EV, Adamson PC, Childhood Absence Epilepsy Study Group. Ethosuximide, valproic acid, and lamotrigine in childhood absence epilepsy. N Engl J Med 2010;362(9):790-799.

Pedley TA, Mendiratta A, Walczak TS. Seizures and epilepsy. In: Ebersole JS, Pedley TA, editors. Current practice of clinical electroencephalography. 3rd ed. Philadelphia: Lippincott, Williams & Wilkins, 2003.

Question 148: Clinical Adult - Sleep

Discussion:

This individual has restless legs syndrome (RLS). RLS is characterized by 1) an urge to move the legs, usually accompanied by uncomfortable or unpleasant leg sensations, 2) symptoms beginning or worsening during rest or inactivity, 3) symptoms occur only, or are worse, in the evening or night compared to the day, 4) symptoms are partially or totally relieved by movement or stretching for at least as long as the activity continues, and 5) symptoms are not solely accounted for as being primary to another condition, such as leg cramps. Behavioral disorders such as impulse control disorders are not associated with RLS but can be seen with other movement disorders such as Parkinson disease.

References:

Allen RP, Picchetti D, Herring WA, et al.. Restless legs syndrome: diagnostic criteria, special considerations, and epidemiology. Sleep Med 2003;4(2):101-119

Silber MH. Sleep-Related Movement Disorders. Continuum Lifelong Learning in Neurol 2013;19(1):170-184

Question 149: Clinical Adult - Neurology of Systemic Disease

Discussion:

For patients with sickle cell disease and stroke, blood transfusions to reduce the hemoglobin S level to under 30% is recommended. Hydroxyurea can be considered in people who cannot undergo transfusions.

References:

Kernan WN, Ovbiagele B, Black HR, Bravata DM, Chimowitz MI, Ezekowitz MD, Fang MC, Fisher M, Furie KL, Heck DV, Johnston SC, Kasner SE, Kittner SJ, Mitchell PH, Rich MW, Richardson D, Schwamm LH. Guidelines for the prevention of stroke in patients with stroke and transient ischemic attack: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. Stroke. 2014;45:2160-2236

Question 161: Clinical Adult - Movement Disorders

Discussion:

Dopamine agonists have been reported to produce a behavioral dyscontrol syndrome in patients with Parkinson disease.

References:

Gschwandtner U, Aston J, Renaud S, Fuhr P. Pathologic gambling in patients with Parkinson's disease. Clin Neuropharmacology 2001;24:170-172.

Black KJ, Friedman JH. Repetitive and impulsive behaviors in treated Parkinson disease. Neurology 2006;67(7):1118-9.

Question 166: Clinical Adult - Neuro-oncology

Discussion:

This patient has post-transplant lymphoproliferative disease (PTLD) resulting from chronic immunosuppression and activation of Epstein-Barr virus (EBV) infection. EBV causes monoclonal transformation of B-lymphocytes and in turn can result in primary CNS lymphoma.

References:

Rosenfeld MR, Pruitt AA. Management of Malignant Gliomas and Primary CNS Lymphoma: Standard of Care and Future Directions. Continuum Lifelong Learning Neurol 2012;18(2):406-415

Question 170: Clinical Adult - Motor Neuron/Nerve

Discussion:

The lateral femoral cutaneous nerve innervates the mid portion of the lateral thigh. In a lateral femoral cutaneous neuropathy the nerve conduction studies would demonstrate a absence or reduced lateral femoral sensory action potential. The EMG should be normal.

References:

Hobson-Webb ,Lisa D and Juel, Vern. CONTINUUM: Lifelong Learning in Neurology: 2017; 23(2) : 487?511.

Question 176: Clinical Adult - Spinal and Root Disorders

Discussion:

The classic presentation of early delayed radiation injury is Lhermitte sign and is characterized by electric shock-like sensation or paresthesia on the spine and limbs upon flexion of the neck. This develops 3 to 4 months after treatment and spontaneously resolves.

References:

By Jing Wu, PHD: Surabhi Ranjan MBBS. Continuum of life long learning, Neoplastic Myelopathies, 2018, 474-496.

Question 188: Clinical Adult - Neuro-ophthalmology/Neuro-otology

Discussion:

Superior canal dehiscence syndrome, first described a few decades ago, presents in several different ways, with either acoustic or vestibular symptoms predominating. It is due to a Valsalva-induced communication between a dehisced superior semicircular canal bone and the intracranial space.

References:

Lempert T, von Brevern M. Episodic vertigo. Curr Opin Neurol 2005;18:5-9.

Question 193: Clinical Adult - Demyelinating Disease

Discussion:

This patient has signs and symptoms of an acute transverse myelitis with a longitudinally extensive lesion by MR imaging. When superimposed on a history of a severe optic neuritis this presentation is most compatible with neuromyelitis optica spectrum disorder (NMO). The NMO antibody (NMO-IgG), an antibody to the aquaporin-4 water channel, is a specific, though not 100% sensitive, marker for neuromyelitis optica.

References:

Tobin, WO; Pittock, SJ. Autoimmune Neurology of the Central Nervous System. CONTINUUM: Lifelong Learning in Neurology: June 2017, volume 23, p 627?653

Goodman BP. Diagnostic Approach to Myeloneuropathy. Continuum Lifelong Learning in Neurology 2011;17(4):2011

Bermel RA, Fox RJ. MRI in Multiple Sclerosis. Continuum Lifelong Learning in Neurology 2010;16(5):37-57

Wingerchuk DM. Neuromyelitis Optica Spectrum Disorders. Continuum Lifelong Learning in Neurology 2010;16(5):105-121

Jarius S, Franciotta D, Bergamaschi R, et al. NMO-IgG in the diagnosis of neuromyelitis optica. Neurology 2007;68(13):1076-1077.

Question 194: Clinical Adult - Movement Disorders

Discussion:

Writer's cramp, a form of focal dystonia, is an activity-specific movement disorder associated with discomfort and abnormal posturing without more generalized symptoms.

References:

Morgante, Francesca MD, PhD; Klein, Christine MD. Dystonia. Continuum: A lifelong Learning in Neurology. 2013;(5):1225-1241

Geyer H, Bressman S. Treatment of Dystonia. Continuum Lifelong Learning Neurol 2007;13(1):94-121.

Question 279: Clinical Adult - Neuro-ophthalmology/Neuro-otology

Discussion:

This patient has nonarteritic anterior ischemic optic neuropathy (NAION) resulting in optic nerve head ischemia. This is usually due to vascular occlusive disease of the posterior ciliary arteries which supply the optic nerve. Embolism from cardiac or large artery sources underlie few if any cases of NAION. In contrast to retinal ischemia, NAION is not associated with carotid occlusive disease. The primary risk factors are hypertension and diabetes mellitus. Most patients awaken with painless monocular visual loss presumably because of nocturnal hypotension. Corticosteroids, hyperbaric oxygen, and anticoagulation are not beneficial for this condition. Abrupt lowering of blood pressure may aggravate the ischemia. No treatment has been shown to improve clinical outcome in these patients but fortunately most will improve or stabilize over several weeks. Aspirin therapy is appropriate as it reduces the patient's future risk of cardiovascular and cerebrovascular disease. Vasculitic anterior ischemic optic neuropathy, a common presentation of giant cell arteritis, usually produces severe monocular or binocular visual loss. It often occurs in association with headache, systemic symptoms and elevated ESR.

References:

Rucker JC, Biousse V, Newman NJ. Ischemic optic neuropathies. Curr Opin Neurol 2004;17(1):27.

Biousse V, Newman N. Retinal and Optic Nerve Ischemia. Continuum Lifelong Learning Neurol 2014;20(4):838-856.

Question 299: Clinical Adult - Infectious Disease

Discussion:

Hematologic malignancies, treatment with chemotherapy and treatment with monoclonal antibodies are risk factors for progressive multifocal leukoencephalopathy. MRI reveals non-enhancing FLAIR abnormalities that involve the white matter more than the gray matter. Diagnosis is made by CSF demonstration of JC virus.

References:

Capone PM, Scheller JM. Neuroimaging of infectious disease. Neurol Clin 2014 Feb;32(1):127-145.

Berger JR, Aksamit AJ, Clifford DB, Davis L, Koralnik IJ, Sejvar JJ, Bartt R, Major EO, Nath A. PML diagnostic criteria: consensus statement from the AAN Neuroinfectious Disease Section.. Neurology. 2013 Apr 9;80(15):1430-8.

Question 302: Clinical Adult - Infectious Disease

Discussion:

Acute bacterial meningitis is characterized by headache, fever, nuchal rigidity, mental status changes and photophobia. Recommended emergent treatment in a patient with a high suspicion of the diagnosis is dexamethasone given simultaneous with or followed by empirical antibiotics. The recommended empirical antibiotics of choice, in this instance, are a 3rd generation cephalosporin and vancomycin, not penicillin. Dexamethasone may reduce mortality and neurologic complications in patients with bacterial meningitis.

References:

van der Beek D, Farrar J, de Gans J, et al. Adjunctive dexamethasone in bacterial meningitis: a meta-analysis of individual patient data. Lancet Neurol 2010;9:254-263.

Roos, KL. Bacterial Infections of the Central Nervous System. Continuum Lifelong Learning in Neurology: December 2015 - Volume 21 - Issue 6, p 1679?1691

de Gans J, van der Beek D. Dexamethasone in adults with bacterial meningitis. European Dexamethasone in Adulthood Bacterial Meningitis Study Investigators. N Engl J Med. 2002;347(20):1549.

Tunkel AR, Hartman BJ, Kaplan BA, et al. Practice Guideline for the Management of Bacterial Meningitis. Clin Inf Dis 2005;39:1267-1284.

Question 309: Clinical Adult - Spinal and Root Disorders

Discussion:

Down syndrome can be associated with atlantoaxial instability. Special precautions must be taken prior to any intubation in order to prevent neurologic damage.

References:

Aminoff MJ, Greenberg DA, Simon RP. Clinical neurology. 6th ed. New York: Lange Medical Books/McGraw-Hill, 2005;225-226.

Question 310: Clinical Adult - Neuromuscular Disorders

Discussion:

This patient most likely has idiopathic brachial neuritis. This disorder is more common in young adults and sometimes follows physical exertion or other physical stress, including upper respiratory tract infection, vaccination, surgery, and childbirth. A small percentage of patients have an autosomal dominantly inherited form of the disorder. Typically, idiopathic brachial plexitis presents with severe pain followed by weakness and sensory loss in the upper extremity. Weakness may occur within 24 hours, but its onset is more commonly delayed two weeks or longer. The prognosis for eventual recovery is good. The role of corticosteroids is not certain, although they often help pain considerably.

References:

Vera Bril, BSc, MD, FRCPC; ; Hans D. Katzberg, MD, MSC, FRCPC;. Acquired Immune Axonal Neuropathies. Continuum 2014;20(5):1261-1273.

Question 312: Clinical Adult - Neurology of Systemic Disease

Discussion:

In patients with cancer, they are at increased risk of thrombotic events (hypercoagulable state). This patient's symptoms evolved over 2 weeks which is not the typical presentation of an intracerebral hemorrhage and thus should raise the possibility of hemorrhage secondary to an acute venous sinus thrombosis. The location of the hemorrhage in the temporal lobe is a common location of hemorrhage from a transverse sinus thrombosis. In a venous sinus thrombosis, the hemorrhage is caused by a backup of blood into the parenchyma because of abnormal blood flow into the venous system and out of the brain. Thus, treatment relies on decreasing clot burden and treating the sinus thrombosis so that normal blood flow is restored. Heparin drip and anticoagulation are therefore, the treatments of choice. In arterial hemorrhage, the efficacy of platelet transfusions and fresh frozen plasma have been called to question in patients with normal coagulation studies and a normal complete blood count.

References:

Kernan WN, Ovbiagele B, Black HR, Bravata DM, Chimowitz MI, Ezekowitz MD, Fang MC, Fisher M, Furie KL, Heck DV, Johnston SC, Kasner SE, Kittner SJ, Mitchell PH, Rich MW, Richardson D, Schwamm LH. Guidelines for the prevention of stroke in patients with stroke and transient ischemic attack: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. Stroke. 2014;45:2160-2236

Question 316: Clinical Adult - Cerebrovascular Disease

Discussion:

Pregnancy is not an absolute contraindication to IV alteplase. In the absence of clear contraindications and given the severity of this patient's symptoms (aphasia and hemiparesis) which are likely to be disabling, IV alteplase should be administered as soon as possible in this patient.

References:

Gartman E. The use of thrombolytic therapy in pregnancy. Obstet Med. 2013 Sep; 6(3): 105?111.

Question 333: Clinical Adult - Neuro-ophthalmology/Neuro-otology

Discussion:

This patient's history is most compatible with a unilateral Adie tonic pupil. An Adie's pupil is typically initially large although becomes smaller over time. It shows minimal reaction to light but normal constriction to near, i.e. light-near dissociation. Unlike normal pupils, which will show no response to instillation of dilute pilocarpine, Adie pupils will constrict to this agent due to denervation super sensitivity from ciliary ganglion dysfunction. Unlike Adie pupils, Argyll-Robertson pupils due to neurosyphilis are typically bilaterally small. Adie pupils are often associated with impaired muscle stretch reflexes; this combination of findings is referred to as the Holmes-Adie syndrome. Apraclonidine is used to detect a Horner pupil which should dilate in response to this agent.

References:

Kawasaki, Aki. Anisocoria. Continuum Lifelong Learning Neurol 2009;15(4):218-235

Busl K, Ropper A. Neurologic consultation in the hospital: hospital consultation for the patient with generalized weakness. Continuum Lifelong Learning Neurol 2011;17(5):1040-1062.

Question 334: Clinical Adult - Neuromuscular Disorders

Discussion:

Eculizumab is a first-in-class humanized monoclonal antibody developed to target the cleavage of C5. It has been shown to be effective in the treatment of paroxysmal nocturnal hemoglobinuria, atypical hemolytic uremic syndrome and most recently in myasthenia gravis. Eculizumab can impair neutrophil and monocyte functions and predispose to encapsulated bacterial infections.

References:

Howard J et. al,. Safety and Efficacy of eculizumab in anti-acethycholine receptor antibody-costive refractory generalized myasthenia gravis (REGAIN): a phase 3, randomized, double-blind placebo controlled multi center. Lancet 2017;16:976-986.

Question 337: Clinical Adult - Movement Disorders

Discussion:

This patient most likely has Whipple disease, a rare multisystem disorder secondary to infection by Tropheryma whipplei, a Gram-positive, non-acid-fast, periodic acid-Schiff (PAS) positive Bacillus. Celiac disease presents with gastrointestinal complaints either in childhood or adulthood, and the principle neurological manifestation is ataxia. Progressive supranuclear palsy and Multiple system atrophy develop in a more subacute to chronic manner with other prominent features. Creutzfeldt-Jakob disease does not usually present with prominent gastrointestinal features.

References:

Eric R. Eggenberger. NYSTAGMUS AND OTHER ABNORMAL EYE MOVEMENTS. Continuum 2009;15(4): 200-212

Swartz, MN. Whipple's disease—past, present, and future. N Engl J Med 2000;342:648.

Question 343: Clinical Adult - Neuro-oncology

Discussion:

A randomized trial published in 2005 demonstrated the benefit of a direct decompressive surgery followed by radiotherapy compared to radiotherapy alone. In patients with acute onset of epidural spinal cord compression, patients who underwent surgery within 24 hours had significant improvement in their ability to walk and the length of time that they were able to continue to walk.

References:

Patchell R, Tibbs P, Regine W et al.. Direct decompressive surgical resection in the treatment of spinal cord compression caused by metastatic cancer: a randomized trial.. Lancet 2005;366:643-648

Question 348: Clinical Adult - Neurotoxicology

Discussion:

This patient has developed a length-dependent sensorimotor polyneuropathy. Metronidazole is associated with a toxic sensorimotor polyneuropathy affecting both large and small fibers. Toxicity is dependent on cumulative dose (usually greater than 30 gm) and recovery is often delayed for 6 to 12 months. The other antibiotics have not been associated with significant adverse peripheral nervous system effects.

References:

Kapor K, Chandra M, Mag D, et al. Evaluation of metronidazole toxocity: a prospective study. Int J Clin Pharmacol Res 1999;19(3):83-88

Morrison B, Choudhry V. Medication, Toxic and Vitamin-Related Neuropathies. Continuum Lifelong Learning in Neurol 2012;18(1):139-160

Question 353: Clinical Adult - Demyelinating Disease

Discussion:

In patients with acute exacerbations of MS who fail to improve with IV methylprednisolone, plasma exchange is a reasonable next step. Steroid-refractory acute exacerbations in MS have been shown to have better outcomes with plasma exchange when compared to those who received sham exchanges. Oral corticosteroids have not been shown to be useful in treating MS exacerbations. There is not an established role for the use of intravenous immunoglobulin (IVIG), cyclophosphamide, or natalizumab in the treatment of acute MS exacerbations.

References:

Weinshenker BG, O'Brien PC, Petterson TM et al.. A randomized trial of plasma exchange in acute central nervous system inflammatory demyelinating disease. Ann Neurol. 1999;46(6). 878-886

Cortese I, Chaudhry V, So YT, Cantor F, et al. Evidence-based guideline update: plasmapheresis in neurologic disorders: report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. Neurology 2011;76(3):294.

Question 355: Clinical Adult - Movement Disorders

Discussion:

Progressive supranuclear palsy typically presents in the seventh decade, with early postural instability, vertical supranuclear gaze palsy, and levodopa-unresponsive parkinsonism. This patient's signs and symptoms of early falls, symmetric Parkinsonism, and

hyperextended neck are most compatible with progressive supranuclear palsy. Dementia with Lewy body presents with dementia and visual hallucinations. Spinocerebellar atrophy has a ataxia as a common presenting sign. Multiple system atrophy presents with prominent autonomic symptoms. Parkinson disease presents with unilateral signs and is responsive to levodopa.

References:

Noseworthy J. Neurological therapeutics: principles and practice. New York: Taylor & Francis, 2006.

Wiliams D, Litvan I.. Parkinsonian Syndromes. Continuum: Lifelong Learning in Neurology 2013;19(5):1189-1212.

Question 359: Clinical Adult - Epilepsy

Discussion:

HLA-B genetic testing is indicated in patients of Han-Chinese, Thais, or Malaysians descent prior to initiation. The HLA-B 1502 allele is predictive of carbamazepine induced severe rash including Steven-Johnson syndrome and toxic epidermal necrolysis and therefore should be tested on patients of Asian descent.

References:

Bassel W Abou-Khalil, MD, FAAN. Continuum Life long learning, Antiepileptic drugs, 2016, 132-156.

Question 366: Clinical Adult - Epilepsy

Discussion:

In utero exposure to Valproic acid is associated with autism spectrum disorder. Studies have shown absolute risk of 4.42% in Valproate-exposed children.

References:

Cynthia L. HArden, MD. Continuum life long learning, Pregnancy and epilepsy, 2014, Page 60-79.

Question 381: Clinical Adult - Neuromuscular Disorders

Discussion:

This patient most likely has hereditary neuropathy with liability to pressure palsies (HNPP). Other choices would be less likely due to the lack of systemic symptoms. The findings of demyelination on the nerve conductions is consistent with HNPP. Patient should have genetic test for HNPP which is due to a duplication in PMP 22.

References:

Chrestian N et, al.. Hereditary neuropathy with liability to pressure palsies in childhood: case series and literature update. Neuromuscul Disord 2015;25(9):693-698.

Amato AA, Russell JA. Neuromuscular disorders. 1st ed. New York: McGraw Hill Medical, 2008.

Question 382: Clinical Adult - Other Pain Syndromes

Discussion:

This patient has idiopathic glossopharyngeal neuralgia. Secondary causes, including skull-based tumors, have been adequately excluded by MRI. Syncope associated with this syndrome results from activation of the carotid sinus branch of the glossopharyngeal nerve, resulting in bradycardia and hypotension due to peripheral arterial vasodilatation. Symptomatic therapy is the same as that used for trigeminal neuralgia.

References:

Gronseth G, Cruccu G, Alksne J, et al. Practice Parameter: the diagnostic evaluation and treatment of trigeminal neuralgia (an evidence-based review). Neurol 2008;71)15):1183-1190.

Rozen T. Trigeminal neuralgia and glossopharyngeal neuralgia. Neurol Clin 2004;22(1):185.

Saper CB. Visceral Sensation and Visceral Sensory Disorders. Continuum Lifelong Learning in Neurol 2007;13(6):204-214.

Question 384: Clinical Adult - Critical Care/Stroke

Discussion:

This patient most likely has thiamine deficiency with Wernicke encephalopathy (WE), which is characterized by delirium, ataxia, and nystagmus, sometimes with ophthalmoplegia. This disorder can be seen in any patient who is severely malnourished. WE can be difficult to distinguish due to its often-nonspecific presentation, and the incomplete triad of classic signs. There is no strong clinical suggestion of serotonin syndrome, hypoglycemia, narcotic overdose or B12 deficiency.

References:

Singh S, Kumar A. Wernicke encephalopathy after obesity surgery: a systematic review. Neurology 2007;68:807-811.

Sechi GP, Serra A. Wernicke Encephalopathy: new clinical settings and recent advances in diagnosis and management. Lancet Neurol 2007;6:442-455

Question 386: Clinical Adult - Neurorehabilitation

Discussion:

Ability to recover upper extremity use in stroke has been looked at in terms of regaining the ability to perform activities of daily living and regain functional independence. Patients most likely to improve with any motor training program for the upper extremity are those who have residual function at the start. No movement in the arm at 15 days, or no ability to grip at one month predict poor functional outcome of the upper extremity. Neglect (in this case mild and likely transient) and a less intensive rehabilitation program are likely to retard patient progress, a plegic arm is felt "unlikely to respond to any currently available motor training program." Hemorrhage dos not predicts a worse outcome and initial complications of stroke do not preclude eventual recovery.

References:

Good DC, Bettermann K, Reichwein RK. Stroke Rehabilitation. Continuum: Lifelong Learning in Neurology 2011; 17(3):545-567.

Question 390: Clinical Adult - Sleep

Discussion:

This patient's symptoms are consistent with cataplexy, an emotionally-induced loss of strength and postural tone. Excessive daytime sleepiness and cataplexy are the most commonly occurring accompaniments of narcolepsy, with hypnagogic hallucinations and sleep paralysis being less common. Other associated symptoms may include vivid dreams, fragmented unrestful nocturnal sleep, automatic behaviors, periodic limb movements of sleep and REM behavior disorder.

References:

Malhotra S, Kushida CA. Primary Hypersomnias of Central Origin. Continuum Lifelong Learning in Neurology 2013:19(1):67-85

Question 391: Clinical Adult - Movement Disorders

Discussion:

This patient's findings of a unilateral resting tremor and cogwheel rigidity, without a history of neuroleptic exposure, are most suggestive of idiopathic Parkinson disease (PD). Symptoms of REM sleep behavior disorder are seen in up to 50% of patients with PD and can predate the motor symptoms of parkinsonism by many years.

References:

Comella CL. Sleep disorders in Parkinson's disease: an overview. Mov Disord 2007;22(S17):S367-S373.

Loddo G et. al,. The treatment of sleep disorders in Parkinson's disease: From research to clinical practice. Front Neurol 2017;8:42

Question 396: Clinical Adult - Other Pain Syndromes

Discussion:

Complex regional pain syndrome type 1 (CRPS 1) is the likely diagnosis. CRPS 1 is most closely associated with trauma to a limb, include acute burning pain, hyperalgesia and allodynia in the absence of any demonstrable nerve injury. Pain is typically remote from and distal to the site of injury. Acutely there may be increased warmth, hyperhidrosis and unilateral distal edema. Symptoms and findings change with the chronic phase of the syndrome. MRI of the limb may demonstrate abnormalities of skin or joints, but these are not specific for CRPS 1. Plain radiographs may show multiple abnormalities in bone but are only useful in the chronic stages of CRPS 1. Quantitative sensory testing may demonstrate abnormal mechanical and thermal sensory thresholds, but these changes are not specific. Skin biopsy, with quantitative and qualitative analysis of small nerve fibers, have shown highly variable results in CRPS 1 and its diagnostic value is unclear. Bone scintigraphy has been shown to be useful in the acute phase of CRPS 1 and may show homogenous unilateral hyper perfusion in the two early phases of the test with increased periarticular radiotracer uptake in the delayed (3 hour) phase.

References:

Naleschinski D, Baron R. Complex regional pain syndrome: evolving understanding of pathogenesis and implications for treatment. Continuum Lifelong Learning Neurol 2009;15:47-57.

Question 397: Clinical Adult - Neuro-oncology

Discussion:

Ma2 antibodies are predominantly found in young males with germ cell tumors. Patients with Ma2 antibodies most often have limbic system encephalitis and eye movement abnormalities, especially paresis of vertical gaze, but can also have cerebellar degeneration. These patients should be evaluated for testicular cancer.

References:

Eric Lancaster, MD, PhD;. Continuum lifelong learning, Paraneoplastic Disorders, Neuro-oncology p. 1653-1679, 2017, Vol.23, No.6.

Clinical Pediatrics

Question 37: Clinical Pediatrics - Infectious Disease

Discussion:

Of the causes of congenital infections listed (CMV, Rubella, HIV, Syphilis, and toxoplasmosis), toxoplasmosis is the most likely to manifest after delivery with liver abnormalities and obstructive hydrocephalus. The physical findings of hydrocephalus in a 1-month-old infant include prominent scalp veins and "sundown" eyes.

References:

Swaiman KF, Ashwal S, Ferriero DM, Schor, NT,Finkel, RS, Gropman, AL , Pearl PL, and Shevell, M editors. Pediatric neurology: principles and practice. 6th ed. Philadelphia: Mosby, 2017.

Question 39: Clinical Pediatrics - Neonatal

Discussion:

Neonatal encephalopathy from hypoxic-ischemia as in this case can injure the basal ganglia / thalamus, cerebral cortex, watershed cortex and white matter, or periventricular / central cerebral white matter. One predominant injury pattern involves the basal ganglia / thalamus, and the other involves the watershed areas. The basal ganglia / thalamus injury pattern occurs with sentinel events such as severe placental abruption. The watershed injury pattern occurs with partial, prolonged disruption of placental perfusion. Periventricular cerebral white matter injury, strokes, and intraventricular hemorrhages can occur hypoxic-ischemia encephalopathy but are less common and less likely in this clinical scenario.

References:

de Vries LS, Cowan FM. Evolving understanding of hypoxic-ischemic encephalopathy in the term infant. Semin Pediatr Neurol 2009;16:216-225

Glass HC. Hypoxic-Ischemic Encephalopathy and Other Neonatal Encephalopathies. Continuum (Minneap Minn) 2018;24:57-71

Volpe JJ. Neonatal encephalopathy: an inadequate term for hypoxic-ischemic encephalopathy. Ann Neurol 2012;72:156-166

Question 42: Clinical Pediatrics - Neonatal

Discussion:

The patient described has a history consistent with glycine encephalopathy (nonketotic hyperglycinemia), given frequent apnea, myoclonus, and burst suppression pattern on EEG. Many mothers will note frequent "hiccups" of the fetus in utero, although this is often only elicited on specific questioning. The diagnosis is made by CSF amino acids, typically compared to serum amino acids, where an elevated glycine level is seen, with an increased ratio of CSF:serum glycine. It can also be detected on intermediate echo MR spectroscopy. While MRI brain may demonstrate corpus callosal abnormalities, these are nonspecific.

Very long chain fatty acids can be elevated in Zellweger syndrome and other peroxisomal disorders.

Urine sulfites are increased in molybdenum cofactor and sulfite oxidase deficiency.

Urine organic acids can determine some causes of neonatal encephalopathy and seizures, such as methylmalonic aciduria and maple syrup urine disease.

References:

Swaiman KF, Ashwal S, Ferriero DM, Schor, NT,Finkel, RS, Gropman, AL , Pearl PL, and Shevell, M editors. Pediatric neurology: principles and practice. 6th ed. Philadelphia: Mosby, 2017.

Question 50: Clinical Pediatrics - Hereditary and Metabolic Disorders

Discussion:

The brief scenario describes a myopathic picture with a suggestion of an evolving neuropathy. Involvement of muscle is a characteristic feature of mitochondriopathies such as cytochrome oxidase type 1 deficiency, as is neuropathy. Congenital disorders of glycosylation would present with failure to thrive, ataxia, seizures, and cerebellar hypoplasia. Glucose transporter deficiency type 1 would present with difficult to control epilepsy. Glutaric aciduria presents with macrocephaly and metabolic crisis, usually in the context of an illness or other metabolic stress. Methylmalonic academia presents as a progressive encephalopathy, episodes of stroke, and hepatomegaly.

References:

Swaiman KF, Ashwal S, Ferriero DM, Schor, NT,Finkel, RS, Gropman, AL , Pearl PL, and Shevell, M editors. Pediatric neurology: principles and practice. 6th ed. Philadelphia: Mosby, 2017.

Question 53: Clinical Pediatrics - Epilepsy

Discussion:

Benign occipital epilepsy (Panayiotopoulos syndrome) is one of the benign focal epilepsies of childhood; with a frequency about half of childhood epilepsy with centrotemporal spikes (CECTS). Autonomic symptoms predominate. In about one in five seizures the child will become flaccid and unresponsive (ictal syncope). Although considered an occipital epilepsy, the interictal EEG may not reveal occipital spikes and the ictal EEG onset may be posterior or anterior. Conventional seizures with eye deviation or motor manifestations also occur.

References:

Covanis A. Panayiotopoulos syndrome: a benign childhood autonomic epilepsy frequently imitating encephalitis, syncope, migraine sleep disorder, or gastroenteritis. Pediatrics 2006;118:1237-1243.

Swaiman KF, Ashwal S, Ferriero DM, Schor, NT,Finkel, RS, Gropman, AL , Pearl PL, and Shevell, M editors. Pediatric neurology: principles and practice. 6th ed. Philadelphia: Mosby, 2017.

Wyllie, Elaine. Wyllie's Treatment of Epilepsy: Principles and Practice. 6th edition. Philadelphia: Wolter Kluwer, 2015

Question 61: Clinical Pediatrics - Neurosurgery, Critical Care and Tumors

Discussion:

Fever and irritability are seen in meningoencephalitis, but the characteristic presentation of spinal epidural abscess is a transverse myelopathy and a flexed posture resisting extension. This is a neurosurgical emergency. While infantile Guillain-Barre syndrome (AIDP) can present with bowel and bladder dysfunction, the posture and irritability would be unusual. Sandifer syndrome is not likely to have bowel and bladder symptoms, and botulism would not present with fever, irritability or flexed posture.

References:

Swaiman KF, Ashwal S, Ferriero DM, Schor, NT,Finkel, RS, Gropman, AL , Pearl PL, and Shevell, M editors. Pediatric neurology: principles and practice. 6th ed. Philadelphia: Mosby, 2017.

Question 66: Clinical Pediatrics - Vascular and Inflammatory Disorders

Discussion:

The patient has a history and examination consistent with acute disseminated encephalomyelitis (ADEM). Features of ADEM include a single polyfocal CNS event with a presumed demyelinating cause. Lesions tend to be bilateral, and affect the deep grey structures and cortex. It is typically preceded by an illness, or occasionally, immunizations. Although ADEM is a diagnosis of exclusion, of the choices it is the most likely diagnosis.

Acute cerebellar ataxia may also affect children of this age and be post-infectious. One would not expect encephalopathy, or the MRI lesions described with this diagnosis.

In prepubertal children, anti-NMDA receptor encephalitis affects males and females equally, and may occur in the postinfectious setting. However, it is more frequently associated with movement disorder, seizures, and sleep disturbances at this age range. Leigh disease is a mitochondrial disorder, and while acute worsening can occur with infection, one would not expect typical development at this age of 4 years. Pediatric MS is equally predominant in prepubertal males and females. However, the distribution of lesions, presence of encephalopathy and lack of dissemination in both time and space makes this less likely.

References:

Swaiman KF, Ashwal S, Ferriero DM, Schor, NT,Finkel, RS, Gropman, AL , Pearl PL, and Shevell, M editors. Pediatric neurology: principles and practice. 6th ed. Philadelphia: Mosby, 2017.

Question 67: Clinical Pediatrics - Vascular and Inflammatory Disorders

Discussion:

The boy in this vignette likely has acute flaccid myelitis (AFM), characterized by acute weakness in >1 limb and either a spinal cord lesion on MRl restricted to the gray matter spanning >1 spinal segments for a confirmed case or a CSF pleocytosis of >5 white blood cells/mm3 for a probable case. Although AFM can occur at any age, most are younger than 21 years old. Asthma is one of the most common comorbidities. Many have a prodromal illness consisting of respiratory or gastrointestinal symptoms during week prior to the onset of neurological symptoms. The weakness shows an asymmetric, lower motor neuron pattern that commonly involves the arms proximally. At least 20% have cranial nerve involvement. Enterovirus D68 has been associated with AFM. Anti-aquaporin 4 antibodies may have a pathological role in neuromyelitis optica spectrum disorders. Elevated serum ferritin is one of the diagnostic criteria for hemophagocytic lymphohistiocytosis.

References:

Messacar K, Schreiner TL, Van Haren K, et al.. Acute flaccid myelitis: A clinical review of US cases 2012-2015. Ann Neurol 2016;80:326-338

Narula S, Banwell B.. Pediatric Demyelination. Continuum (Minneap Minn) 2016;22:897-915

Question 80: Clinical Pediatrics - Neuromuscular

Discussion:

While weakness has multiple causes, the physical findings here are most consistent with dermatomyositis. A muscle biopsy would show perifascicular atrophy with sparing of the central fascicle, along with perivascular inflammation. The skin features would be unusual in a viral myositis, and Duchenne muscular dystrophy does not have such findings. Kawasaki disease would have other dermatologic manifestations. SLE would likely have a classic malar rash.

References:

Swaiman KF, Ashwal S, Ferriero DM, Schor, NT,Finkel, RS, Gropman, AL , Pearl PL, and Shevell, M editors. Pediatric neurology: principles and practice. 6th ed. Philadelphia: Mosby, 2017.

Question 93: Clinical Pediatrics - Cerebral Palsy

Discussion:

Prenatal or postnatal middle cerebral artery infarction is the most common cause of congenital hemiparesis. About 1/6000 uncomplicated live births have an arterial infarction. In most instances no clear etiologic factors can be identified. Children are usually normal at birth, although those with perinatal infarctions may manifest seizures, usually restricted to the hand. Far less commonly encountered etiologies include subdural hemorrhage, arteriovenous malformations, or hemimegalencephaly, and in such instances additional findings or a more eventful history are often encountered. Unilateral infantile venous sinus thrombosis is rare and is seldom an occult process.

References:

Swaiman KF, Ashwal S, Ferriero DM, Schor, NT,Finkel, RS, Gropman, AL , Pearl PL, and Shevell, M editors. Pediatric neurology: principles and practice. 6th ed. Philadelphia: Mosby, 2017.

Question 110: Clinical Pediatrics - Movement Disorders

Discussion:

GTP cyclohydrolase deficiency may produce abnormalities of tone and movement that result in a Parkinsonian syndrome. An additional diagnostic clue is the occurrence of repeated bouts of otherwise unexplained hyperthermia. Congenital disorder of glycosylation, cytochrome oxidase deficiency, multiple sulfatase deficiency, and succinic semialdehyde dehydrogenase deficiency do not have a prominent associated movement disorder.

References:

Swaiman KF, Ashwal S, Ferriero DM, Schor, NT,Finkel, RS, Gropman, AL , Pearl PL, and Shevell, M editors. Pediatric neurology: principles and practice. 6th ed. Philadelphia: Mosby, 2017.

Question 116: Clinical Pediatrics - Hereditary and Metabolic Disorders

Discussion:

Notably, the infant's head size is well below normal. Of the choices provided, only lissencephaly is associated with microcephaly and epileptic spasms. Perinatally acquired cytomegalovirus infection (CMV) is not generally associated with infantile spasms. Fragile X syndrome is usually not associated with infantile spasms. Tuberous sclerosis is frequently a cause of infantile spasms but is not generally associated with microcephaly. Aicardi syndrome generally does not occur in boys. The diagnosis of cryptogenic infantile spasms implies no other abnormalities are found, which is not consistent with severe microcephaly.

References:

MacKay MT, Weiss SK, Adams-Webber T, et al. Practice parameter: Medical treatment of infantile spasms: Report of the American Academy of Neurology and the Child Neurology Society. Neurology 2004;62:1668-1681.

Wyllie, Elaine. Wyllie's Treatment of Epilepsy: Principles and Practice. 6th edition. Philadelphia: Wolter Kluwer, 2015

Question 126: Clinical Pediatrics - Neuromuscular

Discussion:

Nemaline myopathy has a static or slowly progressive course with rod-like inclusions on trichrome studies. Creatine kinase is normal or mildly elevated; EMG may be normal. The most common cause is a mutation in the alpha-actin gene. Fukuyama muscular dystrophy would not have the noted inclusions, nor would Mersin-deficient myopathy. Mitochondrial myopathy would show ragged red fibers. SMA type III would not present with a normal EMG

References:

Swaiman AF, Ashwal S, Ferriero DM, Schor NF. Swainman's pediatric neurology. Principles and practice. 5th ed. Philadelphia: Elsevier, 2012.

Question 131: Clinical Pediatrics - Headache/Other Paroxysmal Disorders

Discussion:

Benign paroxysmal torticollis is classified as a migraine equivalent by the International Headache Society. Some children go on to develop basilar-type migraines. Sandifer syndrome is posturing from esophageal discomfort and usually involves the trunk. Spasmus nutans has ocular oscillations along with head tilt, and dopa-responsive dystonia usually begins after 5 years of age, typically in the foot.

References:

Swaiman KF, Ashwal S, Ferriero DM, Schor, NT,Finkel, RS, Gropman, AL , Pearl PL, and Shevell, M editors. Pediatric neurology: principles and practice. 6th ed. Philadelphia: Mosby, 2017.

Question 154: Clinical Pediatrics - Develop, Learn, Lang, Behav, Psych Disorders

Discussion:

Narcolepsy consists of a diagnostic tetrad that includes excessive daytime sleepiness, cataplexy, hypnagogic or hypnopompic hallucinations, and sleep paralysis. The most common presenting symptom in children is excessive daytime sleepiness, which in children and young adults may precede the development of cataplexy by several years. Diagnosis of narcolepsy is usually made when a positive multiple sleep latency test (MSLT) is found in individuals who experience both excessive daytime weakness and cataplexy.

References:

Swaiman KF, Ashwal S, Ferriero DM, Schor, NT,Finkel, RS, Gropman, AL , Pearl PL, and Shevell, M editors. Pediatric neurology: principles and practice. 6th ed. Philadelphia: Mosby, 2017.

Question 165: Clinical Pediatrics - Develop, Learn, Lang, Behav, Psych Disorders

Discussion:

Both conditions may manifest ESES. By definition regressive autism occurs prior to three years of age, while the peak age of language loss with Landau-Kleffner syndrome is 5-7 years of age. Although behavioral and cognitive dysfunction may be found in Landau-Kleffner, these appear to be the result of language dysfunction, while they arise with equal primary significance in autistic regression. Prognosis for recovery is worse with earlier age of onset for both conditions. 75% of children with Landau-Kleffner manifest seizures, whereas convulsive seizures are far less common in children with autistic regression.

References:

Swaiman KF, Ashwal S, Ferriero DM, Schor, NT,Finkel, RS, Gropman, AL , Pearl PL, and Shevell, M editors. Pediatric neurology: principles and practice. 6th ed. Philadelphia: Mosby, 2017.

Question 185: Clinical Pediatrics - Epilepsy

Discussion:

Childhood Epilepsy with Centrotemporal Spikes (CECTS) is characterized by onset between 5 and 7 years of age, nocturnal occurrence, and benign interictal neurologic examination, and a characteristic EEG with independent Centro-temporal spikes with a horizontal dipole. It remits completely by adolescence in about 80% of patients, although other epileptic syndromes, including juvenile myoclonic epilepsy (JME), have been seen in some patients. Childhood absence remits in about two-thirds of children, although a few develop generalized convulsive epilepsy in adolescence or adulthood. JME often requires prolonged or indefinite treatment, with only about 20% remitting. Infants with prolonged febrile seizures followed by multiple seizure types are often manifesting Dravet syndrome and respond poorly to treatment. Lennox-Gastaut syndrome rarely remits and is often intractable.

References:

Wyllie, Elaine. Wyllie's Treatment of Epilepsy: Principles and Practice. 6th edition. Philadelphia: Wolter Kluwer, 2015

Questions 196 - 200: Clinical Pediatrics - Cerebral Palsy

Discussion:

While kernicterus has become less common in developed countries due to monitoring of maternal Rh and ABO sensitization and neonatal bilirubin, it has not disappeared. In a home delivery without prenatal or neonatal medical supervision, risk is increased of maternal sensitization, unrecognized bilirubin encephalopathy, but also undetected inborn errors such as glutaric aciduria. Typical features of kernicterus are early hypotonia, followed by opisthotic posturing and later athetoid/dystonic Cerebral palsy with lack of vertical gaze, sensorineural hearing loss, but preserved intelligence. Infants with glutaric aciduria typically deteriorate markedly after a minor illness causing a catabolic state. Developed countries now test for glutaric aciduria on neonatal screening, but even with awareness of diagnosis and need to avoid fasting, patients may deteriorate abruptly or gradually. Pelizaeus-Merzbacher syndrome is associated with coarse nystagmus, lack of myelination diffusely on MRI. It can be either

recessive or X-linked. Lesch-Nyhan syndrome is associated with severe self-injurious behavior and chorea, but onset is later than the perinatal period. Lesions of kernicterus may be inapparent on CT or even on MRI, but there may be cystic changes in globus pallidus with high signal on T2-weighted images. Juvenile Huntington disease more often presents with bradykinesia and dystonia, not usually chorea. MELAS and Kearns-Sayre syndrome may present with a variety of findings, but symmetric chorea or athetosis would be unusual. HIV encephalopathy, if untreated, typically causes loss of motor function, usually with spasticity as the major component. PKAN is generally characterized by progressive dystonia.

References:

Swaiman KF, Ashwal S, Ferriero DM, Schor, NT,Finkel, RS, Gropman, AL , Pearl PL, and Shevell, M editors. Pediatric neurology: principles and practice. 6th ed. Philadelphia: Mosby, 2017.

Question 258: Clinical Pediatrics - Epilepsy

Discussion:

The lesion is a hypothalamic hamartoma. Typical presentation is gelastic epilepsy (seizures beginning with mirthless laughter). Endocrine effects are relatively uncommon, but precocious puberty may occur. None of the other seizure types described would be a consequence of a lesion in this location and with this appearance.

References:

Wyllie, Elaine. Wyllie's Treatment of Epilepsy: Principles and Practice. 6th edition. Philadelphia: Wolter Kluwer, 2015

Question 304: Clinical Pediatrics - Epilepsy

Discussion:

Although any of these conditions may result in neurologic deterioration, epilepsy is not a prominent element of any of the conditions listed save for glucose transporter type I deficiency (DeVivo disease). Persistent and worsening seizures and encephalopathy are hallmarks of this disease due to energy failure, which can effectively be treated with the ketogenic diet.

References:

Swaiman KF, Ashwal S, Ferriero DM, Schor, NT,Finkel, RS, Gropman, AL , Pearl PL, and Shevell, M editors. Pediatric neurology: principles and practice. 6th ed. Philadelphia: Mosby, 2017.

Wyllie, Elaine. Wyllie's Treatment of Epilepsy: Principles and Practice. 6th edition. Philadelphia: Wolter Kluwer, 2015

Question 306: Clinical Pediatrics - Neurosurgery, Critical Care and Tumors

Discussion:

Eleven percent of pediatric brain tumors are pilocytic astrocytomas, and 80% are cystic. Medulloblastomas are rarely cystic, and glioblastoma multiforme is rare in this age group and in this location. Dandy-Walker malformations usually present in the first year of life. Cysticercosis in the posterior fossa most often presents extra-axially, and the enhancement is usually ring-like.

References:

Swaiman KF, Ashwal S, Ferriero DM, Schor, NT,Finkel, RS, Gropman, AL , Pearl PL, and Shevell, M editors. Pediatric neurology: principles and practice. 6th ed. Philadelphia: Mosby, 2017.

Question 308: Clinical Pediatrics - Hereditary and Metabolic Disorders

Discussion:

Labhart-Prader-Willi presents with hypotonia, small size and usually poor feeding. A prolonged delivery with assistance required is quite common. Hyperphagia and secondary obesity occur later and can be partially corrected with dietary regulation and growth hormone supplementation. SMA I patients have absent reflexes. Patients with Sotos syndrome demonstrate macrocephaly, metachromatic leukodystrophy presents with absent or very diminished reflexes and may have Babinski signs, and Zellweger syndrome presents with very significant hepatomegaly.

References:

Swaiman KF, Ashwal S, Ferriero DM, Schor, NT,Finkel, RS, Gropman, AL , Pearl PL, and Shevell, M editors. Pediatric neurology: principles and practice. 6th ed. Philadelphia: Mosby, 2017.

Question 318: Clinical Pediatrics - Develop, Learn, Lang, Behav, Psych Disorders

Discussion:

The combination of poor visuospatial skills, poor comprehension with good rote reading and memorization, and difficulty with peer relationships, at least partly due to inability to "read" faces, is typical for nonverbal learning disabilities. This is sometimes termed "right hemisphere learning disability," but anatomic localization is not clear.

Angelman syndrome would be associated with epilepsy and poorer language function. Apraxia is associated with more motor difficulties. Dyslexia is associated with poor sight reading. Children with attention deficit hyperactivity disorder have difficulty with rote memory.

References:

Volden, J. nonverbal Learning Disability. Handbook of Clinical Neurology 2013; 111: 245-249

Waber, DP. Rethinking Learning Disabilities. New York: Guilford Press, 2011

Question 324: Clinical Pediatrics - Neuromuscular

Discussion:

The congenital myasthenic syndromes are not related to an immune process but are caused by genetic defects affecting the neuromuscular junction. These include defects in acetylcholine synthesis and packaging (familial infantile myasthenia gravis), end-plate deficiency of acetylcholinesterase, acetylcholine receptor deficiency, and the slow channel syndrome.

References:

Swaiman KF, Ashwal S, Ferriero DM, Schor, NT,Finkel, RS, Gropman, AL , Pearl PL, and Shevell, M editors. Pediatric neurology: principles and practice. 6th ed. Philadelphia: Mosby, 2017.

Question 331: Clinical Pediatrics - Neonatal

Discussion:

The standard of care for neonates born at 36 weeks gestational age or older with neonatal encephalopathy from suspected or confirmed hypoxia-ischemia is 72 hours of therapeutic hypothermia at 33.5C. The eligibility criteria include having a gestational age of at least 35-36 weeks at birth, moderate to severe encephalopathy on exam, and at least one indicator of perinatal distress. Indicators of distress include an Apgar score below 5 at 10 minutes, an umbilical cord blood gas of less than 7.00 or base excess of -12 to -16 or more in the first hour of life, or more than 10 minutes of resuscitation. Therapeutic hypothermia should be implemented within the first 6 hours of life. The reduction in death or major neurodevelopmental disability with therapeutic hypothermia is about 25%.

References:

Committee on Fetus and Newborn. Hypothermia and neonatal encephalopathy. Pediatrics 2014;133:1146-1150

Glass HC. Hypoxic-Ischemic Encephalopathy and Other Neonatal Encephalopathies. Continuum (Minneap Minn) 2018;24:57-71

Question 332: Clinical Pediatrics - Headache/Other Paroxysmal Disorders

Discussion:

Pain may result in excessive vagal tone and bradycardia or asystole with ensuing pallid breath-holding. Cyanotic breath-holding is usually provoked by anger or frustration. Central hypoventilation syndrome is associated with sleep. Some occipital epileptic syndromes show light provocation. Paroxysmal choreoathetosis can be provoked by movement initiation. Paroxysmal torticollis is not usually emotionally or sensorially induced.

References:

Swaiman KF, Ashwal S, Ferriero DM, Schor, NT,Finkel, RS, Gropman, AL , Pearl PL, and Shevell, M editors. Pediatric neurology: principles and practice. 6th ed. Philadelphia: Mosby, 2017.

Question 341: Clinical Pediatrics - Neuromuscular

Discussion:

The patient described has a history concern for a glycogen storage disease, type V (GSD V), caused by an enzymatic defect on myophosphorylase encoded by PYGM on 11q13. This metabolic myopathy is characterized by exercise intolerance, myalgias, and muscle cramps. Patients can have myoglobinuria and rhabdomyolysis after extreme activity. Unlike other causes of episodic myoglobinuria, CK can remain elevated between episodes. EMG is typically normal, and forearm exercise test can be diagnostic. While the patient strenuously clenches and unclenches the hand, ammonia, lactate and pyruvate levels are obtained at multiple intervals.

A normal response shows a 3 to 4-fold increase in ammonia, lactate and pyruvate from baseline, while patients with GSD V will have an appropriate rise in ammonia with no rise in lactate or pyruvate. Those with poor effort do not show a rise in any values.

Patients with lactate dehydrogenase deficiency will have the expected rise of ammonia and pyruvate, but no rise in lactate. Finally, patients with fatty acid oxidation defects may or may not have myopathic motor unit potential and demonstrate a rise in lactate and pyruvate with no rise in ammonia.

References:

Tabon, Alejandro. Metabolic Myopathies.. Continuum: Lifelong Learning in Neurology. Volume 19, Issue 6 Muscle Disease (2013).

Question 350: Clinical Pediatrics - Headache/Other Paroxysmal Disorders

Discussion:

The majority of children with recurrent headaches, with complete clearing between episodes, do not need neuroimaging. The following would mandate neuroimaging in a child presenting with headaches: auras lasting more than an hour, persistent neurologic findings, abnormal neurologic exam between headaches, predominantly occipital headaches, loss of vision at headache peak, decline in cognitive function, decline in growth velocity, or recent significant change in headache pattern.

References:

Silberstein S, Lipton R, Dodick D, editors. Wolff's headache and other head pain. 8th ed. New York: Oxford University Press, 2008.

Question 360: Clinical Pediatrics - Hereditary and Metabolic Disorders

Discussion:

Hypertrophic obstructive cardiomyopathy is the characteristic cause of death in Friedreich ataxia. Smaller numbers of patients may succumb to complications of diabetes. Lymphoma and other consequences of immunodeficiency occur at increased rates in ataxia-telangiectasia, another recessively inherited progressive ataxic syndrome. Respiratory failure and status epilepticus do not occur more commonly in Friedreich ataxia compared to the population at large.

References:

Swaiman KF, Ashwal S, Ferriero DM, Schor, NT,Finkel, RS, Gropman, AL , Pearl PL, and Shevell, M editors. Pediatric neurology: principles and practice. 6th ed. Philadelphia: Mosby, 2017.

Question 363: Clinical Pediatrics - Develop, Learn, Lang, Behav, Psych Disorders

Discussion:

The young woman has late juvenile metachromatic dystrophy, which presents as neuropsychiatric symptoms with relatively subtle motor signs, including her ataxia, incipient neuropathy, dysarthria, and long tract signs. Arylsulfatase A determination would confirm the diagnosis. Galactocerebrosidase deficiency (Krabbe disease) in its late juvenile form has more fulminant motor signs. A CMA is not likely to be helpful here, and a mitochondriopathy (lactate and pyruvate determinations) would not likely present in this fashion. Organic acidemias would likely present with metabolic crises after intercurrent illness, and not subacute neuropsychiatric disease.

References:

Swaiman KF, Ashwal S, Ferriero DM, Schor, NT,Finkel, RS, Gropman, AL , Pearl PL, and Shevell, M editors. Pediatric neurology: principles and practice. 6th ed. Philadelphia: Mosby, 2017.

Question 365: Clinical Pediatrics - Infectious Disease

Discussion:

Bartonella is generally spread by cats, particularly feral kittens that live outdoors or in barns. Status epilepticus is a rare complication and can be difficult to treat. Occasionally demyelinating lesions are caused by Bartonella. Neuroborreliosis and babesiosis do not usually present with convulsive status epilepticus. Tuberculous meningitis presents with elevated CSF protein. Malaria is not endemic in the temperate United States.

References:

Nelson, C et al.. Cat-scratch Disease in the United States, 2005-2013. Emerg. Inf. Dis. 2016; 22(10):1741-1746

Question 369: Clinical Pediatrics - Headache/Other Paroxysmal Disorders

Discussion:

Spasmus nutans usually begins in the first year of life. Children are neurologically normal, although some may have coexisting amblyopia or strabismus. The triad of abnormal head position(s), head nodding, and nystagmus is characteristic, although not all components need be present simultaneously, and the nystagmus may sometimes be monocular. The major differential diagnosis is tumors of the optic apparatus. Another important distinction is between the abnormal eye movements observed with spasmus nutans and the chaotic but conjugate saccadic eye movements frequently seen in children with neuroblastoma associated with ataxia and myoclonus. The syndrome usually remits in 1 to 2 years.

References:

Swaiman KF, Ashwal S, Ferriero DM, Schor, NT,Finkel, RS, Gropman, AL , Pearl PL, and Shevell, M editors. Pediatric neurology: principles and practice. 6th ed. Philadelphia: Mosby, 2017.

Question 370: Clinical Pediatrics - Epilepsy

Discussion:

While corpus callosotomy can be used in intractable epilepsy, this is more effective for drop attacks (akinetic seizures). Most epileptologists suggest this in this situation only after the failure of other options to improve seizure control, including vagus nerve stimulation, ketogenic diet, and felbamate. In a patient who has failed multiple drugs, the ketogenic diet has a higher response rate than a new anticonvulsant. The three listed medications may actually worsen generalized epilepsy and are less likely to succeed.

References:

Wyllie, Elaine. Wyllie's Treatment of Epilepsy: Principles and Practice. 6th edition. Philadelphia: Wolter Kluwer, 2015

Question 375: Clinical Pediatrics - Develop, Learn, Lang, Behav, Psych Disorders

Discussion:

The patient described above has symptoms consistent with attention deficit hyperactivity syndrome, combined type. She has features of inattention (daydreaming, easily distracted) and hyperactivity (fidgety, excessive talking). Symptoms are present in two settings (home and school), and she has a potentially positive family history. ADHD is associated with several behavioral disorders, including Oppositional Defiant Disorder, Conduct Disorder, depression and anxiety. The former two are more common in those with hyperactivity subtype, while the latter two are seen more in inattentive or combined subtypes. Although the patient is reported to have staring spells, based on the clinical history, this is likely behavioral, rather than due to absence seizures, for example. While juvenile myoclonic epilepsy and childhood epilepsy with centrotemporal spikes can have associated behavioral concerns or can be seen in patients with ADHD, these are not considered coexisting disorders.

References:

Swaiman KF, Ashwal S, Ferriero DM, Schor, NT,Finkel, RS, Gropman, AL , Pearl PL, and Shevell, M editors. Pediatric neurology: principles and practice. 6th ed. Philadelphia: Mosby, 2017.

Question 377: Clinical Pediatrics - Neurosurgery, Critical Care and Tumors

Discussion:

Cerebellar mutism is a frequent postoperative problem in children who have had posterior fossa surgery, particularly tumor resections that split the vermis. Initially, the child is most often mute other than crying. Behavioral state may initially be akinetic but awake, with marked apathy to the environment evolving to marked agitation. As the child improves, marked dysarthria is noted, with initially very sparse speech. Although the child improves, cognitive and behavioral sequelae are often seen.

References:

Gudrunardottir, T. et al.. Consensus paper on post-operative pediatric cerebellar mutism syndrome: The Iceland Delphi results. Childs Nervous System 2016;32(7): 1195-1203

Question 378: Clinical Pediatrics - Neurosurgery, Critical Care and Tumors

Discussion:

Medulloblastomas are a type of primitive neuroectodermal tumor arising in the cerebellum, most often occurring in the fourth ventricle. The typical neuroimaging is of a tumor that is dense on noncontrast CT and diffusely enhances on CT or MRI. MR spectroscopy characteristically has high choline peak, taurine peak, and low to absent N-acetylaspartate. So-called average risk medulloblastomas are those that do not have evidence of leptomeningeal spread at the time of diagnosis and have been completely or nearly completely surgically resected.

References:

Siegfried, A et al.. Clinical, pathological and molecular data on desmoplastic/nodular medulloblastomas. Clinical Neuropathology 2016;35(3): 106-113

Finlay JL, Packer RJ, Erdreich-Epstein A. Progress in the treatment of childhood brain tumors: no room for complacency. Pediatr Hematol Oncol 2007;24:79-84.

Question 379: Clinical Pediatrics - Movement Disorders

Discussion:

Bradykinesia and rigidity are more common than choreoathetosis in childhood or juvenile Huntington disease, and most patients have rapid progression to death after symptom onset. The white matter is unaffected. Oculomotor signs are not common. Seizures occur in about 50% of patients but are a late finding.

References:

Swaiman KF, Ashwal S, Ferriero DM, Schor, NT,Finkel, RS, Gropman, AL , Pearl PL, and Shevell, M editors. Pediatric neurology: principles and practice. 6th ed. Philadelphia: Mosby, 2017.

Question 398: Clinical Pediatrics - Vascular and Inflammatory Disorders

Discussion:

Head and neck injuries, even quite mild, may be accompanied by significant arterial injury. In this instance, the localization would lead one to diagnose a left pontomedullary stroke, and neck flexion which produced dissection of one vertebral artery would be the likeliest mechanism. Diffuse axonal injury would be unlikely to be associated with these findings, as would concussion. Epidural hemorrhage can present with a lag between occurrence and symptoms, but the localization of these findings would be unusual for such an event. The same would be true for subdural hemorrhage.

References:

Swaiman KF, Ashwal S, Ferriero DM, Schor, NT,Finkel, RS, Gropman, AL , Pearl PL, and Shevell, M editors. Pediatric neurology: principles and practice. 6th ed. Philadelphia: Mosby, 2017.

Contemporary Issues

Question 59: Contemporary Issues - Ethics/Professionalism

Discussion:

Although advances in understanding the pathophysiology of ALS have stimulated the development of new drug therapies, the mainstay of treatment for ALS patients remains symptomatic management. The AAN Practice Parameter on the care of the patient with ALS recommends frequent discussions of the goals of care because decision making may be subject to change as the disease becomes more severe. Between 40% and 73% of patients experience pain in later stages of ALS, and AAN guidelines recommend use of opioids when non-narcotic treatment fails. While the use of carefully titrated benzodiazepines to alleviate anxiety and respiratory distress is indicated, the use of neuromuscular blockade is not supported by AAN guidelines. Few patients on long-term invasive ventilation regret their choice, but because patient satisfaction is higher with noninvasive than invasive ventilation, noninvasive ventilation should be considered first.

References:

Miller RG, Rosenberg JA, Gelinas DF. Practice parameter: the care of the patient with amyotrophic lateral sclerosis. Report of the Quality Standards Subcommittee of the American Academy of Neurology. Neurology 1999;52:1311-1323. http://www.neurology.org/cgi/reprint/52/7/1311.pdf [accessed February 7, 2011]

Question 68: Contemporary Issues - Ethics/Professionalism

Discussion:

In emergency circumstances where irreversible harm or death would occur by withholding requested treatment, it is best to initiate the treatment and then seek consultation from an ethics committee. An ethics consultation can rarely be done immediately as there would be insufficient time to gather the information necessary to offer a recommendation. Refusals to treat on the basis of medical futility require a due process of evaluation of the patient's interests, the family's wishes, and the medical facts of the case, including prognosis. Medical futility cannot be determined unilaterally without ethics consultation. Anencephaly is not equivalent to brain death, as there is function of the brain stem and there are respiratory efforts.

References:

Anomynous. In the matter of baby "K" No. 93-1899, No. 93-1923, No. 93-1924. United States Court of Appeals 16F.3d590; 1994 US app. (LEXIS 2215).

Question 73: Contemporary Issues - Practice

Discussion:

Core competency of professionalism. In this case, the resident is responsible for the medication error and should acknowledge the error. At the very least, the patient's hospital stay will be prolonged while waiting for the phenytoin levels to fall into the safe range. The attending physician should be made aware of the error, and steps taken to ensure better communication with the ED to prevent future medication errors. The patient should be informed of the error and what problems, if any, can be expected. While it is uncomfortable to admit an error, most patients appreciate being informed and in fact are less likely to initiate a lawsuit if their physicians communicate with them.

References:

ACGME core competencies to be provided.. http://www.acgme.org/acWebsite/home/home.asp; 7-31-09

Question 104: Contemporary Issues - Evidence-based Medicine

Discussion:

Only random error can be reduced by increasing sample size. The other three types or error listed are all examples of systematic error (or bias). If there is a systematic problem with the data being collected, then increasing the sample size will only result in the collection of more data with the same systematic problem.

References:

Guyatt G, Rennie D, Meade MO, Cook DJ, Jaeschke R.. Users' Guides to the Medical Literature (Chapter 5. Why Study Results Mislead: Bias and Random Error). JAMAevidence: http://jamaevidence.com/abstract

Question 112: Contemporary Issues - Business

Discussion:

Although states may have unique telemedicine requirements, 48 states, the District of Columbia, Puerto Rico, and the US Virgin Islands all require that physicians engaging in telemedicine are licensed in the state in which the patient is located.

References:

Federation of State Medical Boards. Telemedicine Policies. www.fsmb.org/globalassets/advocacy/key-issues/telemedicine_policies_by_state.pdf accessed July 2018

Question 128: Contemporary Issues - Evidence-based Medicine

Discussion:

The case-control study design begins with the outcome and then asks about exposure and nonexposure. The cohort study design designs begin with exposure and then ask about outcome (disease). Randomized trials are not observational studies.

References:

Evidence Based Medicine. 7/2014 https://www.aan.com/education/ebm/

Question 137: Contemporary Issues - Driving

Discussion:

The laws governing driving privileges after a seizure are enacted and enforced by state agencies whose attempts to assign risk on the basis of these various data have generated complex, sometimes unclear, and nationally nonuniform standards. Single unexplained convulsions with loss of consciousness usually necessitate cessation of driving for some interval, although epilepsy is not as yet diagnosed. Some patients with epilepsy are permitted in some jurisdictions to drive if, in the judgment of the treating neurologist, there is high likelihood that all seizures will occur in sleep. Individuals with epilepsy who have remained seizure free for intervals varying from 3 to 12 months (depending on state of residence) may be permitted to resume driving. The responsibilities of the neurologist include clarifying history and diagnosis, providing appropriate treatment, being aware of driving standards within his/her own and possibly other states, and explaining these standards to the patient, including the necessity of reporting certain events and diagnoses. Neurologists customarily complete portions of the forms patients are mandated to file with state agencies at intervals stipulated by state laws in order to continue driving.

References:

Epilepsy.com site with state links. http://www.epilepsy.com/epilepsy/rights_driving 8-09

Krauss GL, Ampaw L, Krumholz A. Individual state driving restrictions for people with epilepsy in the US.. Neurology 2001; 57:1780-1785.

Question 184: Contemporary Issues - Practice

Discussion:

Drug companies seeking FDA approval to sell a new prescription medication in the United States must test it in various ways. First are laboratory and animal tests. Next are tests in humans to see if the drug is safe and effective when used to treat or diagnose a disease. After testing the medication, the company then sends FDA an application called a New Drug Application (NDA). Some drugs are made out of biologic materials. Instead of an NDA, new biologic drugs are approved using a Biologics License Application (BLA). Whether an NDA or a BLA, the application includes the drug's test results manufacturing information to demonstrate the company can properly manufacture the drug the company's proposed label for the drug. The label provides necessary information about the drug, including uses for which it has been shown to be effective, possible risks, and how to use it. If a review by FDA physicians and scientists shows the drug's benefits outweigh its known risks and the drug can be manufactured in a way that ensures a quality product, the drug is approved and can be marketed in the United States.

References:

FDA Basics. http://www.fda.gov/AboutFDA/Transparency/Basics/default.htm.

Question 336: Contemporary Issues - Ethics/Professionalism

Discussion:

Huntington disease is an autosomal dominant trait with complete penetrance, and offspring from affected patients have a 50% chance of developing the disease. Most patients become symptomatic in the third or fourth decade. Presymptomatic testing for Huntington disease should be performed only voluntarily at the request of an at-risk patient. Genetic testing should be

accompanied by pretest and posttest counseling. Guidelines are available and emphasize voluntariness, confidentiality, safety, absence of coercion, and availability of counseling.

References:

Case adapted from American Academy of Neurology Ethics, Law and Humanities Committee. Ethical Dimensions of Neurologic Practice: A case-based curriculum for neurology residents. March 2000.

Went L. Ethical issues policy statement on Huntington's disease molecular genetics predictive test. International Huntington Association. World Federation of Neurology. J Med Genet 1990:27;34-38.

Question 345: Contemporary Issues - Practice

Discussion:

Injuries sustained by abused persons can cause chronic neck and back pain, and migraines or other headache types. Clinicians need to have a high level of suspicion in unexplained trauma cases, especially with changing stories and physical contradictory evidence.

References:

Coker A, Smith P, Bethea L, et al. Physical health consequences of physical and psychological intimate partner violence. Arch Fam Med 2000;9:451?457.

Question 358: Contemporary Issues - Business

Discussion:

The 10-point review of systems is an important part of practice management and is required by CMS for the physician to be reimbursed at a level 5. The 10-system review must be performed and carefully documented in order to qualify a history as comprehensive. Although a social history is required, only one element needs to be documented, even for a comprehensive level visit.

References:

US Dept of Health and Human Services. Welcome to Medicare Exam. http://www.cms.hhs.gov/WelcometoMedicareExam/

Question 361: Contemporary Issues - HIPAA

Discussion:

Per recent privacy rules, appropriate release should be obtained from the parents or custodian of a minor before divulging clinical information. The Health Insurance Portability and Accountability Act (HIPAA) was signed into law August 21, 1996. The medical records of a minor may not be released or discussed with other family members without the written consent of the child's legal guardian, most often the parent, but not always (USDHHS, 2008).

References:

United States Department of Health and Human Services. Office for Civil Rights - HIPAA Medical Privacy - National Standards to Protect the Privacy of Personal Health Information. Available from: http://www.hhs.gov/ocr/hipaa/.[Accessed 1-09]

Question 373: Contemporary Issues - Business

Discussion:

Time-based billing requires that the provider documents spending over 50% of the face-to-face visit either coordinating care or counseling the patient. Twenty minutes is exactly at 50% and therefore does not meet the requirement.

References:

Centers for Medicare & Medicaid Services. 2017. Available from https://www.cms.gov/Medicare/Coding/MedHCPCSGenInfo/HCPCS_Coding_Questions.html

Question 387: Contemporary Issues - HIPAA

Discussion:

The US federal HIPAA legislation specifically permits organ procurement organization coordinators to review information without consent.

References:

United States Department of Health and Human Services. Health Information Privacy and Civil Rights Questions & Answers; Disclosure to Family and Friends. http://healthprivacy.answers.hhs.gov/cgi-bin/hipaa.cfg/php/enduser/ std_alp.php.

United States Department of Health and Human Services Office for Civil Rights--HIPAA. Standards for Privacy of Individually Identifiable Health Information [45 CFR Parts 160 and 164]. http://www.hhs.gov/ocr/hipaa/guidelines/guidanceallsections.pdf.

Question 392: Contemporary Issues - Evidence-based Medicine

Discussion:

Clinical equipoise, also known as the principle of equipoise, involves assigning patients to different treatment arms of a clinical trial. Randomly assigning subjects to one or another treatment arms is only justified if collective uncertainty in the community exists regarding the efficacy of a particular treatment. It would not be appropriate to randomly assign subjects to receive (or not) a therapy with proven efficacy. Equipoise is also not related to an individual's lack of knowledge about treatment options nor related to establishing guidelines for management options.

References:

Evidence Based Medicine. 7/24/09 http://www.aan.com/education/ebm/

Neuroimaging

Question 202: Neuroimaging - Tumors/Cysts

Discussion:

The lesion involves the splenium and demonstrates homogenous enhancement and diffusion restriction. Abscess may demonstrate diffusion restriction but typically shows ring enhancement. GBM typically does not demonstrate diffusion restriction and typically shows ring enhancement. The lesion does not fit a vascular territory to suggest ischemic stroke, and though ischemic stroke may demonstrate enhancement, this is a subacute finding, at which point ADC darkness would be unlikely to persist. The location is atypical for metastasis. Metronidazole toxicity can affect the selenium but does not cause this extent of enhancement.

References:

Klein JP, Dietrich J. Neuroradiologic Pearls for Neuro-oncology. Continuum December 2017, Vol.23, No.6

Question 203: Neuroimaging - Metabolic, Movement, CSF Circulatory Disorders

Discussion:

The sagittal T1-weighted image shows a small pons and cerebellar atrophy. The axial T2-weighted image shows the pons to be reduced in size with a 'hot cross bun sign.' This finding is not characteristic of cerebellar alcoholic toxicity, spinocerebellar ataxia, type 3 (Machado-Joseph syndrome), fragile X tremor ataxia syndrome, or progressive supranuclear palsy.

References:

Bakshi R, Lindsay BD, Kinkel PR. Brain magnetic resonance imaging in clinical neurology. In: Joynt RJ, Griggs RC, editors. Baker's clinical neurology. Philadelphia: Lippincott, Williams & Wilkins, 1998;1(4A).

Nabatame H, Fukuyama H, Akiguchi I, et al. Spinocerebellar degeneration: qualitative and quantitative MR analysis of atrophy. J Comput Assist Tomogr 1988;12(2):298-303.

Question 204: Neuroimaging - Spine

Discussion:

Epidural lipomatosis is the preferred response. There is significant fat posterior to thecal sac and the fat suppression post-contrast image shows that the signal of the epidural mass suppresses. Epidural hemorrhage has variable signal intensity but would not suppress on fat suppression sequences. Dural arteriovenous fistula would show vascular flow voids and not uniform thickening of the fat. Leptomeningeal carcinomatosis would demonstrate thick, irregular nerve root enhancement. The vertebral bodies are unremarkable, without hyperintensity suggestive of hemangioma.

References:

Yasuda T, Suzuki K, Kawaguchi Y, et al.. Clinical and imaging characteristics in patients undergoing surgery for lumbar epidural lipomatosis.. BMC Musculoskeletal Disorders. 2018;19:66. doi:10.1186/s128

Question 206: Neuroimaging - Spine

Discussion:

The MRI views demonstrate a mass lesion extending into the anterior spinal canal at the L4-L5 interspace level. The imaging featured is typical of a large disc extrusion, and while a neurofibroma can on occasion look similar to a disc extrusion, this lesion is continuous with the L4-L5 disc, and on that basis is far more likely that etiology. The disc likely impinges the traversing L5 root and exiting L4 nerve root. The other choices, including lymphoma and metastatic disease, are highly unlikely to appear continuous with a disc herniation, or have the same signal characteristics as a disc herniation.

References:

Harnsberger HR, Osborn AG, MacDonald A, et al, editors. Diagnostic and Surgical Imaging Anatomy: Brain, Head & Neck, Spine. Salt Lake City: Amirsys, 2006.

Atlas S. Magnetic resonance imaging of the brain and spine. 3rd ed. Philadelphia: Williams and Wilkins, 2002.

Question 208: Neuroimaging - Spine

Discussion:

The mass lesion with isointense signal on T1- and bright T2-weighted signal posterior to the dens is most frequently due to pannus. The inflammatory pannus involving the dens is often seen in association with rheumatoid arthritis.

References:

Greenberg JO. Neuroimaging: a companion to Adams and Victor's principles of neurology. New York: McGraw-Hill, 1999.

Question 210: Neuroimaging - Tumors/Cysts

Discussion:

Anaplastic astrocytoma is the best diagnosis. Anterior cerebral artery infarction would have a more abrupt onset. Intraparenchymal metastasis would be expected to have a focus of intense contrast enhancement surrounded by edema. Meningioma would enhance intensely and would exert extra-axial mass effect. This lesion in intra-axial. Arteriovenous malformation has T2-hypointense flow-voids and more avid enhancement.

References:

Faehndrich J, Weidauer S, Pilatus U, Ozvald A, Zanella FE, Hattingen E. Neuroradiological Viewpoint on the Diagnostics of Space-Occupying Brain Lesions. Clinical Neuroradiology 2011;21:123-139.

Question 211: Neuroimaging - Dementia

Discussion:

Frontotemporal dementia is characterized by a strong gradient of atrophy from anterior to posterior along the temporal lobe, as seen in the patient images. In Alzheimer disease, atrophy occurs throughout the temporal lobe. Binswanger disease is characterized by subcortical foci of patchy T2 hyperintensities in white matter, a finding not seen in the patient images. Although there is ventriculomegaly, it is in proportion to the cortical atrophy, making normal pressure hydrocephalus an unlikely diagnosis in this case. The regional pattern of atrophy is not characteristic of dementia with Lewy bodies.

References:

Libon DJ, Price CC, Garrett KD, Giovannetti T. From Binswanger disease to leuokoaraiosis: what we have learned about subcortical vascular dementia. Clin Neuropsychol 2004;18(1):83-100.

Taber KH, Hurley RA. Herpes encephalitis in the immunocompetent adult: advances in neuroimaging. J Neuropsychiatry Clin Neurosci 2010;22(2):125-129.

Kim EJ, Rabinovici GD, Seeley WW, et al. Patterns of MRI atrophy in tau positive and ubiquitin positive frontotemporal lobar degeneration. J Neurol Neurosurg Psychiatry 2007;78:1375-1378.

O'Brien JT. Role of imaging techniques in the diagnosis of dementia. Br J Radiol 2007;80 Spec No 2:S71-S77.

Question 212: Neuroimaging - Dementia

Discussion:

The pattern of decreased metabolism in the association cortex of the parietal and temporal lobes and in the retrosplenial region is characteristic of Alzheimer disease. Corticobasal degeneration shows decreased metabolism in the association cortex of one hemisphere but not the other, with a marked hemispheric asymmetry not present in this case. Diffuse Lewy body disease is associated with occipital hypometabolism. Frontotemporal lobar degeneration is associated with decreased frontal metabolism. Vascular dementia does not typically show such symmetric, regional predilection.

References:

Masdeu JC, Zubieta JL, Arbizu J. Neuroimaging as a marker of the onset and progression of Alzheimer's disease. J Neurol Sci 2005;236:55-64.

Question 213: Neuroimaging - Metabolic, Movement, CSF Circulatory Disorders

Discussion:

Thyroid associated ophthalmopathy (Grave ophthalmopathy) is an autoimmune inflammatory condition of the orbit associated with hyper- or hypothyroidism. The typical order of predilection for involvement of the extraocular muscles is inferior > medial

> superior > lateral > oblique. This MRI scan demonstrates enlargement of several extraocular muscles, especially the left inferior rectus.

References:

Blaser S, Illner A, Castillo M, et al. Pocket Radiologist PedsNeuro Top 100 Diagnoses. 1st ed. Salt Lake City: Amirsys, 2003.

Question 214: Neuroimaging - Tumors/Cysts

Discussion:

There is a single, large infiltrative multicystic enhancing mass with vasogenic edema. This appearance is most frequently seen with a glioblastoma multiforme. No vascular structures are seen as expected in an arteriovenous malformation (AVM). An infectious process, such as toxoplasmosis and a metastasis, would more likely have a ring pattern of enhancement and not the large complex multicystic pattern seen here.

References:

Greenberg JO, editor. Neuroimaging: a companion to Adams and Victor's principles of neurology. 2nd ed. New York: McGraw-Hill, 1999.

Question 216: Neuroimaging - Spine

Discussion:

There is cerebellar tonsillar ectopia (approximately 1 cm below the foramen magnum) with an associated cervical syrinx, findings consistent with Chiari 1 malformation. The contents of the syrinx correspond to CSF (i.e. T1 hypointense and T2 hyperintense). The lesion has distinct margins and displaces rather than infiltrates adjacent spinal cord. Astrocytomas are infiltrating tumors. Basilar invagination refers to narrowing of the foramen magnum due to upward migration of the top of the C2 vertebrae. MS causes demyelinating lesions of the brain and spinal cord and is not associated with tonsillar ectopia. Chordomas are tumors of notochord remnants which most often occur in the clivus and sacrococcygeal regions.

References:

Klein JP. A practical approach to spine imaging. Continuum (Minneap Minn). 2015;21(1 Spinal Cord Disorders):36-51.

Question 219: Neuroimaging - Metabolic, Movement, CSF Circulatory Disorders

Discussion:

Caudate atrophy is the main radiologic feature of Huntington disease and is present. Hepatic encephalopathy, in addition to diffuse atrophy has a striking increase in the signal intensity of the basal ganglia on T1 weighted images, for which such an image was not presented. Multi-infarct dementia demonstrates multiple chronic infarcts. Parkinson disease has no specific CT findings. Wernicke Korsakoff CT findings may present with hypodensity in periaqueductal gray matter, mammillary bodies, and medial thalamus.

References:

Stober T et al. Bicaudate diameter--the most specific and simple CT parameter in the diagnosis of Huntington's disease. Neuroradiology. 26(1):25-8, 1984.

Question 222: Neuroimaging - Dementia

Discussion:

The small T2 hyperintensities in the axial section correspond to elongated structures on sagittal sections at the same level, noticeable on the T1 and FLAIR images. These structures are bright on T2, but dark on T1 and FLAIR, suggesting the presence of free water. They are not venules, which would be very noticeable in the susceptibility weighted image. If they were arterioles,

the flow void would make them appear as dark dots, even as similar size arteries appear in the subarachnoid space. They are dilated Virchow-Robin or perivascular spaces, around perforating arterioles or venules. Lacunar infarctions are unlikely to be so small and sharply demarcated. They would be bright on FLAIR. Some of the areas that are bright on FLAIR, around the dilated perivascular spaces, could be areas of ischemia or of venous congestion. Hemosiderin deposits would appear dark on T2.

References:

Kirkpatrick JB, Hayman LA. White-matter lesions in MR imaging of clinically healthy brains of elderly subjects: possible pathologic basis. Radiology 1987;162:509-511.

Question 225: Neuroimaging - Tumors/Cysts

Discussion:

The images show a large, briskly-enhancing sellar mass extending into the suprasellar region, which causes compression of the optic chiasm. There is no apparent extension from the internal carotid artery to suggest aneurysm. Tools-Hunt syndrome would not have such circumscribed, homogenous enhancement. Craniopharyngioma would have more heterogenous enhancement and cystic features. Epidermoid and Rathke cleft cysts do not typically enhance so briskly.

References:

Osborne A. Diagnostic imaging: brain. Philadelphia: Elsevier, 2004.

Question 226: Neuroimaging - Developmental/Neurogenetic Disorders

Discussion:

The figures demonstrate multiple subependymal nodules isointense to grey matter. These features are most frequently seen with a setting of a migrational defect of neurons on route from the ventricular zone to the cortical surface. Migration errors are frequently associated with epilepsy as in this case.

References:

Atlas S. Magnetic resonance imaging of the brain and spine. 3rd ed. Philadelphia: Williams and Wilkins, 2002.

Question 227: Neuroimaging - Critical Care/Stroke

Discussion:

The large pituitary mass has hyperdensity on the CT as seen with an acute hemorrhage. The mass shows increase T1- and T2-weighted signal typical of recent hemorrhage. The mass also shows contrast enhancement typical of a large pituitary tumor. The combination of these findings is consistent with a pituitary apoplexy.

References:

Greenberg JO, editor. Neuroimaging: a companion to Adams and Victor's principles of neurology. 2nd ed. New York: McGraw-Hill, 1999.

Question 228: Neuroimaging - Multiple Sclerosis/Autoimmune Disorders (Non-MS)

Discussion:

The diffusion-weighted views demonstrate multiple focal areas of acute infarction. These involve both the deep gray and white matter along with scattered cortical areas of infarction. These regions of infarction are in a multifocal vascular distribution atypical for branch large vessel disease and similarly atypical for small vessel infarctions or a cardioembolic etiology, which tend to be cortical. An MRA scan of the head performed concomitant with the study illustrated demonstrated marked beading along numerous arterial structures typical of vasculitis. This is best seen and illustrated in Figure 3 on the conventional cerebral angiogram.

References:

Pomper MG, Miller TJ, Stone JH, et al. CNS vasculitis in autoimmune disease: MR imaging findings in correlation with angiography. AJNR Am J Neuroradiol 1999;20:75-85.

Question 230: Neuroimaging - Critical Care/Stroke

Discussion:

The CT demonstrates air in a serpiginous pattern in the sulci consistent with venous air embolism. This can arise from traumatic central line removal. Lumbar puncture can cause intracranial hypotension which would not have this appearance, RCVS could cause convexal SAH (which would be hyperdense rather than hypodense), orthopedic surgery can cause fat embolism (which would appear as infarction and/or hemorrhage), endocarditis can cause stroke, mycotic aneurysm, and hemorrhage, none of which are seen here.

References:

J. G. Heckmann, C. J. Lang, K. Kindler, W. Huk, F. J. Erbguth, and B. Neundorfer,. Neurologic Manifestations of Cerebral Air Embolism as a Complication of Central Venous Catheterization. Crit Care Med 2000;28: 1621-5.

Question 232: Neuroimaging - Spine

Discussion:

Spinal dural arteriovenous fistula is the commonest vascular lesion of the spine, accounting for about 70% of spinal vascular lesions. 5-fold more common in males, with mean age of 55-60 years at presentation. Fistula exposes the cord venous drainage to arterial pressure, resulting in chronic cord hypoxia and venous congestion. If prolonged, there will be progressive myelopathy. Symptom onset is typically slowly progressive with weakness and pain which may ascend. MR imaging is important to recognize the cord swelling and hyperintensity with abnormal flow voids due to the fistula in the subarachnoid space. Spinal angiography to identify the fistula is confirmatory and provides access for catheter-based components of therapy when appropriate. Astrocytoma typically has a longer clinical onset with pain prominent. Syringomyelia and subacute combined degeneration do not cause abnormal vascular structures on the surface of the cord. Transverse myelitis has a more rapid pace than spinal dural arteriovenous fistula.

References:

Krings T, Geibprasert S. Spinal Dural Arteriovenous Fistula. AJNR Am J Neuroradiol 2009; 30:639-48

Jellema K, Tijssen CC, van Gijn J.. Spinal dural arteriovenous fistulas: a congestive myelopathy that initially mimics a peripheral nerve disorder. Brain 2006, 129, 3150?3164

Question 235: Neuroimaging - Tumors/Cysts

Discussion:

This extra-axial lesion diffusely and homogenously enhances with contrast. It sits on the dura. The morphology and location make the diagnoses of acoustic neurinoma and trigeminal schwannoma less likely. Astrocytoma and hemangioma are intra-axial tumors. This is an en plaque variant meningioma.

References:

Mohr JP, Gautier JC, editors. Guide to clinical neurology. New York: Churchill Livingstone, 1995.

Question 236: Neuroimaging - Infection

Discussion:

The juxta ventricular lesion is characteristic of the vesicular stage of neurocysticercosis: a spherical cystic lesion with eccentric calcification (scolex) with no surrounding edema. All other answer choices would be expected to have surrounding edema and would be unlikely to have this cystic appearance with eccentric calcification

References:

Raibagkar P, Berkowitz AL. The Many Faces of Neurocysticercosis.. J Neurol Sci. 2018 Jul 15; 390:75-76

Question 237: Neuroimaging - Metabolic, Movement, CSF Circulatory Disorders

Discussion:

Necrosis of the globus pallidus is the most common brain injury occurring in carbon monoxide poisoning and is usually bilateral and symmetric. Methanol poisoning has different appearance with diffuse subcortical white matter lucency and bilateral putaminal infarctions that are often hemorrhagic. The findings of Wernicke encephalopathy are likely not visible on CT but would be seen on MR as periaqueductal and dorsal midbrain, mammillary body, and bilateral thalamic T2 hyperintensity. Hepatic encephalopathy is similarly better seen on MR with T1 hyperintensity in globus pallidus and subthalamic regions. Wilson disease does not demonstrate hypodensities in the globus pallidus such as in this case and may demonstrate atrophic changes in the basal ganglia, cortical and cerebellar regions.

References:

Hegde AN, Mohan S, Lath N, Lim CCT. Differential diagnosis for bilateral abnormalities of the basal ganglia and thalamus. Radiographics 2011;31:5-30.

Sharma P, Eesa M, Scott JN. Toxic and acquired metabolic encephalopathies: MRI appearance. AJR Am J Roentgenol 2009;193(3):879-886.

Question 238: Neuroimaging - Multiple Sclerosis/Autoimmune Disorders (Non-MS)

Discussion:

The figures demonstrate enhancement of the left optic nerve at the junction of the optic nerve and the globe and not the long segment as seen on this study. These are the imaging features seen with acute optic neuritis. Bartonella infection (catscratch disease) is frequently associated with a small focus of enhancement at the disc optic nerve. An orbital cavernoma can present as an intra or extra conal mass; it would not be expected to result in a diffuse pattern of enhancement of the optic nerve. Similarly, orbital pseudotumor is associated with intra or extra corneal inflammatory tissues and not isolated enhancement of the optic nerve.

References:

Greenberg JO, editor. Neuroimaging: a companion to Adams and Victor's principles of neurology. 2nd ed. New York: McGraw-Hill, 1999.

Question 239: Neuroimaging - Tumors/Cysts

Discussion:

This scan demonstrates contrast enhancement in the cerebellar folia and surrounding the upper pons, characteristic of leptomeningeal carcinomatosis.

References:

Question 242: Neuroimaging - Developmental/Neurogenetic Disorders

Discussion:

Dandy-Walker malformation is characterized by incomplete formation of the vermis. markedly elevated torcula, and associated enlargement of the posterior fossa. Joubert's syndrome has a distinct recognizable morphology characterized by abnormal development of midbrain structures (resembling a 'molar tooth'.) Posterior fossa arachnoid cysts have normal vermis. Chiari 2 has a towering cerebellum and small posterior fossa. Medulloblastoma is characterized by intraparenchymal mass lesion typically in the midline cerebellum.

References:

Osborn A, Blaser S, Saltzman K, editors. Diagnostic imaging: brain. Salt Lake City: Amirsys, 2004.

Question 243: Neuroimaging - Infection

Discussion:

The CT and MRI studies demonstrate a cystic defect within the left anterior frontal region. The marked decreased density and lower than water density would be typical of air. Similarly, the marked loss of signal on the T1-weighted study is characteristic of air and lower than signal that is seen due to CSf. A lipoma would have increased signal on the T1-weighted sequence and higher density than seen on the CT scan. An empyema is an infection within the subdural or epidural space and is not present on this study. A porencephalic cyst would have greater density more typical of CSF and higher signal, as is also the case for an abscess.

References:

Atlas S. Magnetic resonance imaging of the brain and spine. 3rd ed. Philadelphia: Williams and Wilkins, 2002.

Question 245: Neuroimaging - Metabolic, Movement, CSF Circulatory Disorders

Discussion:

The location of the T2 hyperintensity in the dorsal midbrain and the symmetrical abnormal enhancement in the mammillary bodies, periaqueductal tissue and dorsal midbrain and the FLAIR hyperintensity in the medial thalami are highly indicative of Wernicke's encephalopathy in this clinical setting. The other entities do produce symmetrical lesions but differ in their combinations of findings.

References:

Smith AB, Smirniotopoulos JG, Rushing EJ, Goldstein SJ. Bilateral thalamic lesions. AJR 2009;192:W53-W62.

Zuccoli G, Gallucci M, Capellades J, et al. Wernicke encephalopathy: MR findings at clinical presentation in twenty-six alcoholic and nonalcoholic patients. AJNR Am J Neuroradiol 2007;28(7):1328-1331.

Question 246: Neuroimaging - Tumors/Cysts

Discussion:

The images depict a large mass within the right cerebellum. This is cystic, with a markedly enhancing nidus or mural nodule. The enhancement is predominately confined to the mural nodule and spares most of the perimeter. There is very mild adjacent vasogenic edema. A metastatic lesion or abscess would be unlikely to demonstrate a mural nodule, and they generally demonstrate a complete ring pattern of enhancement. This appearance can be seen in a setting of a pilocystic astrocytoma; however, this lesion is a frequent finding in youth and highly unlikely in a patient of this age. Medulloblastomas tend to arise in the midline along the margin of the fourth ventricle between the brain stem and cerebellum and not laterally as in this instance and would not have the cystic appearance with a mural nodule. An arteriovenous malformation frequently demonstrates an

enhancing nidus with multiple vascular structures. The vessels in an AVM however, are significantly larger as compared to the capillary size vessels seen here. This lesion is also known as a capillary hemangioblastoma as was confirmed on pathologic examination. Hemangioblastoma is a component of Von Hippel Lindau syndrome, which is also associated with renal cell carcinoma, as occurred in this patient.

References:

Osborn AG, Salzman KL, Barkovich AJ. Diagnostic imaging: brain. 2nd ed. Philadelphia: Amirsys/Lippincott Williams and Wilkins, 2010.

Question 248: Neuroimaging - Infection

Discussion:

The images show bilateral mesial temporal and hippocampal edema, and this and the clinical history supports diagnosis of herpes simplex encephalitis. This disease often leads to elevated RBC count in CSF due to hemorrhagic changes. JC Virus is seen in PML, a white matter disease. HTLV antibodies are seen in HTLV-associated Myelopathy/TSP. Elevated spirochete IgM levels can be seen in CNS Lyme Disease, which causes multifocal white matter lesions. Toxoplasmosis causes focal cerebritis rather than diffuse edema in the temporal lobes.

References:

Rowland, LP. Merritt's neurology. 11th ed. Philadelphia: Lippincott Williams & Wilkins, 2005.

Question 249: Neuroimaging - Critical Care/Stroke

Discussion:

The CT shows a wedge-shaped hemorrhage along the left sylvian fissure, in conjunction with extensive subarachnoid hemorrhage within the sulci, fissures, and cisterns. The pattern is typical of a subarachnoid hemorrhage arising from an aneurysm along the distal internal carotid, or proximal middle cerebral, artery.

References:

Greenberg JO, editor. Neuroimaging: a companion to Adams and Victor's principles of neurology. 2nd ed. New York: McGraw-Hill, 1999.

Question 250: Neuroimaging - Spine

Discussion:

The spinal cord extends down to the sacral level and is attached to a large sacral lipoma which has isointense signal to the patient’s subcutaneous fat. There is a dysraphism of the sacrum also seen on this study. A chordoma is a tumor mass that arises in the sacrum not behind it. Spondylolisthesis is the displacement of one vertebra relative to the one adjacent to it. Chronic inflammatory polyneuropathy demonstrates thickened Cauda equine nerve roots.

References:

Atlas S. Magnetic resonance imaging of the brain and spine. 3rd ed. Philadelphia: Williams and Wilkins, 2002.

Question 253: Neuroimaging - Tumors/Cysts

Discussion:

The correct answer is lipoma. The MRI shows an intradural extramedullary mass which is fairly homogenous and is T1 hyperintense and STIR hypointense. The STIR sequence suppresses fat signal, suggesting that this mass is composed of fat. The other answer choices are lesions which are either not composed of fat or not found in the intradural extramedullary space.

References:

Al-Okaili RN, et al. Advanced MR Imaging Techniques in the Diagnosis of Intraaxial Brain Tumors in Adults. RadioGraphics 2006;26:S173?189

Question 254: Neuroimaging - Infection

Discussion:

The CT study demonstrates profound cortical atrophy with ventriculomegaly on an ex vacuo basis along with calcifications along the ependymal margin. This is a frequent finding in a setting of congenital cytomegalovirus infections. Fahr's disease is an idiopathic disorder with calcifications involving the basal ganglia, the cerebellar, dentate nuclei, and at times, the cortical ribbon, which is not the pattern seen. There is no evidence of an obstruction of the ventricular system seen. Congenital herpes encephalitis results in encephalomalacia involving the mesial temporal, parasagittal, frontal, and insular cortical regions, which is not the pattern seen here. Mitochondrial cytopathies are not associated with ependymal calcifications, as in this case.

References:

A. James Barkovich and Charles Raybaud. Pediatric neuroimaging. 5th ed. Philadelphia: Lippincott, Williams & Wilkins, 2012.

Question 255: Neuroimaging - Metabolic, Movement, CSF Circulatory Disorders

Discussion:

Colloid cyst is the best response because the culprit lesion for this patient's acute hydrocephalus is the hyper dense lesion that has acutely obstructed outflow from both lateral ventricles, resulting in their acute enlargement and ballooning of third ventricle that causes effacement of the interpeduncular and suprasellar cisterns. The scan does not show a visible subarachnoid bleed, and SAH does not explain the dense lesion in the anterior superior third ventricle. The patient does not have fever or neck stiffness to suggest bacterial meningitis, and the course has been for several weeks and bacterial meningitis does not explain the dense lesion in the anterior superior third ventricle. Pituitary apoplexy because the hyperdense lesion in situated the anterior superior third ventricle. Pseudotumor cerebri does not produce obstructive hydrocephalus.

References:

Humphries RL, Stone CK, Bowers RC.. Colloid cyst: a case report and literature review of a rare but deadly condition.. J Emerg Med. 2011 Jan;40(1):e5-9.

Jarquin-Valdivia AA, Rich AT, Yarbrough JL, Thompson RC.. Intraventricular colloid cyst, hydrocephalus and neurogenic stunned myocardium.. Clin Neurol Neurosurg. 2005 Aug;107(5):361-5.

Question 257: Neuroimaging - Spine

Discussion:

The studies demonstrate homogenous enhancement of the cauda equina with suggestion of mild thickening of the nerve roots. This pattern can be seen in conjunction with Guillain-Barrè Syndrome, chronic inflammatory demyelinating polyneuritis, leptomeningeal carcinomatosis, granulomatous disease, or lymphomatosis. There is no evidence of a tethered cord or low-lying conus. B12 deficiency results in lesions within the posterior column and the spinal cord not seen on this study. Ruptured dermoid can result in lipid particles distributed throughout the neuraxis which are not seen on this study. Neurofibromatosis is typically characterized by more thickening of involved nerve roots.

References:

Osborn AG, Ross J, Crim J, et al, editors. Brain and Spine. 1st ed. Philadelphia: Lippincott Williams & Wilkins, 2008.

Question 259: Neuroimaging - Multiple Sclerosis/Autoimmune Disorders (Non-MS)

Discussion:

Multiple sclerosis plaques are shown. This study is FLAIR-weighted and depicts periventricular focal lesions with a pattern typical of so-called "Dawson's fingers" and juxtacortical focal lesions.

References:

Osborn A. Diagnostic neuroradiology. St. Louis: Mosby, 1994.

Question 262: Neuroimaging - Epilepsy

Discussion:

A complex formation of flow voids are seen in the left posterior temporal lobe. No significant surrounding edema is seen. These are most characteristic of arteriovenous malformations.

References:

Osborne A. Diagnostic imaging: brain. Philadelphia: Elsevier, 2004.

Question 265: Neuroimaging - Critical Care/Stroke

Discussion:

The mass lesion has heterogenous T2-weighted and T1-weighted signal characteristic of chronic hemorrhage with hemosiderin. The lesion has a speckled or popcorn appearance typical of a cavernous angioma or cavernoma. An aneurysm has a smooth margin and more homogenous central hemorrhagic pattern. A developmental venous anomaly typically has a 'caput medusae' configuration. A hemorrhagic metastasis is unlikely because of lack of enhancement and vasogenic edema.

References:

Greenberg JO, editor. Neuroimaging: a companion to Adams and Victor's principles of neurology. 2nd ed. New York: McGraw-Hill, 1999.

Question 266: Neuroimaging - Critical Care/Stroke

Discussion:

The CT perfusion images demonstrate increased mean transit time, reduced blood flow, and reduced blood volume suggesting a completed infarct. In the case of ischemia without completion of an infarct, blood flow and volume would be relatively spared. Luxury perfusion is characterized by decreased mean transit time, increased blood flow, and increased blood volume, but those findings are not present on these studies.

References:

Srinivasan A, Goyal M, Al Azri F,Lum C.. State-of-the-Art Imaging of Acute Stroke. Radiographics 2006;26:S75-S95.

Question 271: Neuroimaging - Spine

Discussion:

Spinal epidural hematoma is the best response, with imaging findings of an extradural collection that is slightly hyperintense on T1 and hyperintense on T2 with some heterogeneous hypointense signal admixed in the thoracic portion of the collection. The axial image further confirms the epidural location of the hematoma, with displacement of the dura and epidural fat by the hematoma, distinguishing the lesion from a subdural collection. Epidural abscess is not the best response because the lesion is

T1-hyperintense, suggestive of blood products. Spinal epidural lipomatosis is not the best response because the collection is not of fat signal intensity, epidural lipomatosis rarely involves the cervical spinal canal, and typically causes symptoms of gradual onset when it occurs. Spinal meningioma is typically intradural extramedullary. The lesion is extra-axial, not compatible with longitudinally extensive transverse myelitis.

References:

Robert H. Thiele, Ziad A. Hage, Daniel L. Surdell, Stephen L. Ondra, H. Hunt Batjer, Bernard R. Bendok. Spontaneous Spinal Epidural Hematoma of Unknown Etiology: Case Report and Literature Review. Neurocrit Care 2008; 9: 242-246

Saleem M. Hussenbocus, Martin J. Wilby, Chris Cain, and David Hall. SPONTANEOUS SPINAL EPIDURAL HEMATOMA: A CASE REPORT AND LITERATURE REVIEW. The Journal of Emergency Medicine 2012; 42 (2): e31-e34.

Question 272: Neuroimaging - Multiple Sclerosis/Autoimmune Disorders (Non-MS)

Discussion:

Multiple, T2-hyperintense lesions are seen, with 2 acute enhancing lesions. This is most consistent with an acute exacerbation of multiple sclerosis. Tumefactive demyelination is characterized by more extensive FLAIR signal abnormality. Balo concentric sclerosis has rings of varying amounts of T2-hyperintensity. Neuromyelitis optica has a predilection for the hypothalamus and area postrema. Acute demyelinating encephalomyelitis is characterized by larger, confluent lesions.

References:

Greenberg JO, editor. Neuroimaging: a companion to Adams and Victor's principles of neurology. 2nd ed. New York: McGraw-Hill, 1999.

Question 274: Neuroimaging - Developmental/Neurogenetic Disorders

Discussion:

Coronal neonatal cranial ultrasound and coronal and axial non-enhanced cranial CT images show fusion of the thalami and continuity of cerebral tissue across the midline with a continuous “horseshoe” monoventricle, rather than a third and two distinct lateral ventricles. This morphology with failure of formation of separate right and left cerebral hemispheres indicates holoprosencephaly. The volume of brain and configuration of the CSF containing structures suggests this patient’s anomaly falls in the range of semilobar holoprosencephaly. Canavan’s is a leukodystrophy associated with large, rather than small head size. Anencephaly is characterized by absence of the major portions of the hemispheres and diencephalon. Hydrocephalus refers to abnormal expansion of the ventricles. Periventricular leukomalacia is characterized by abnormal loss of white matter in the peritrigonal region.

References:

Blaser S, Illner A, Castillo M, et al. Pocket Radiologist PedsNeuro Top 100 Diagnoses. 1st ed. Salt Lake City: Amirsys, 2003.

Question 277: Neuroimaging - Critical Care/Stroke

Discussion:

The combination of the patient's physical exam and neuroimaging findings is consistent with a right anterior choroidal artery infarction. The anterior choroidal artery is a branch of the internal carotid artery and supplies the posterior limb of the internal capsule and the lateral thalamus. The paramedian thalamic artery is a branch of the posterior cerebral artery and supplies the medial thalamus. The ophthalmic artery is a branch of the internal carotid artery and supplies the retina.

References:

Greenberg JO, editor. Neuroimaging: a companion to Adams and Victor's principles of neurology. 2nd ed. New York: McGraw-Hill, 1999.

Question 280: Neuroimaging - Tumors/Cysts

Discussion:

The figure demonstrates widening of the CSF space posterior to the spinal cord in the mid thoracic region, resulting in anterior displacement and compression of the cord at that level best seen on the T2 weighted view with somewhat ovoid appearance. This is also well demonstrated as a region of isointense signal to CSF on the T1 weighted views and shows no enhancement. The most common etiology of this appearance is that of a thoracic arachnoid cyst. An epidermoid cyst is an additional, although less likely, etiology and not one of the choices. A lipoma in this location would have increased T1 weighted signal similar to subcutaneous fat tissue not seen here. Similarly, a meningioma would not show the very bright T2 weighted signal and the hypodense signal on T1 weighted view. Myelomalacia within the cord may develop, although is not depicted on this study. The signal of characteristics are not hemorrhage as would be seen in a intrathecal hematoma.

References:

Atlas S. Magnetic resonance imaging of the brain and spine. 3rd ed. Philadelphia: Williams and Wilkins, 2002.

Question 281: Neuroimaging - Tumors/Cysts

Discussion:

Central neurocytoma is the best diagnosis, based on lesion morphology, location, signal intensity and contrast enhancement pattern. Central neurocytomas are located in the ventricles near the foramen of Monro and characteristically have attachment to the septum pellucidum, as shown in this case. Choroid plexus papillomas and meningiomas enhance intensely, and do not assume this morphology that is so characteristic of central neurocytoma. Colloid cyst does not typically enhance. Lymphoma is not typically an intraventricular lesion, but instead infiltrates subependymal tissue and surrounds the ventricles, if involvement is near the ventricles.

References:

Shin JH, Lee HK, Khang SK, et al. Neuronal tumors of the central nervous system: radiologic findings and pathologic correlation. Radiographics 2002;22:1177-1189.

Question 282: Neuroimaging - Metabolic, Movement, CSF Circulatory Disorders

Discussion:

There is gadolinium enhancement of pachymeningeal structures, suggesting hypotension, carcinomatosis or lymphoma. The smooth, diffuse enhancement, together with low-lying tonsils appreciated on the sagittal image, are most consistent with CSF hypotension. The other entities listed can cause pachymeningeal enhancement that is typically more irregular.

References:

Mokri B. Spontaneous cerebrospinal fluid leaks: from intracranial hypotension to cerebrospinal fluid hypovolemia-evolution of a concept. Mayo Clin Proc 1999;74:1113-1123.

Question 283: Neuroimaging - Critical Care/Stroke

Discussion:

The images demonstrate diffusion restriction of the cortical ribbon and basal ganglia consistent with hypoxic-ischemic injury. Subarachnoid hemorrhage would be expected to demonstrate blood in the subarachnoid space on neuroimaging rather than symmetrical intraparenchymal ischemic changes. Embolic ischemic stroke would not be expected to involve the entire cortex and basal ganglia. Bacterial meningitis would be expected to show leptomeningeal enhancement; parenchymal abnormalities, if seen could include abscess, cerebral edema, or stroke, but would not be expected to cause diffuse symmetric diffusion restriction. HSV encephalitis typically causes edema in limbic regions and would not be expected to show diffuse symmetric diffusion restriction.

References:

Greer DM. Cardiac Arrest and Postanoxic Encephalopathy. Continuum 2015, Vol.21, No.5: 1384-1396

Question 285: Neuroimaging - Epilepsy

Discussion:

The figures demonstrate nodular tissue with signal characteristics similar to cortical grey matter adjacent to the lateral ventricles. These tissues are characteristic of subependymal heterotopia that occur as a result of a premature arrest of neuronal migration. This can result as an in utero insult or on a genetic basis. Cortical sulcation is present and not smooth as in lissencephaly nor is there an abnormal cleft as seen in schizencephaly.

References:

A. James Barkovich and Charles Raybaud. Pediatric neuroimaging. 5th ed. Philadelphia: Lippincott, Williams & Wilkins, 2012.

Question 286: Neuroimaging - Metabolic, Movement, CSF Circulatory Disorders

Discussion:

Aqueductal stenosis is preferred response as the expected CSF signal in the aqueduct is not visible, and there is no flow through the aqueduct in either the diastolic (would be dark at aqueduct) or systolic (would be white at aqueduct) phases. Dandy-Walker malformation, Chiari II, and remote subarachnoid hemorrhage are not the best responses because the fourth ventricle is normal. Pontine glioma is not the best response as the pons is normal with no lesion.

References:

Linninger AA, Xenos M, Zhu DC, Somayaji MR, Kondapalli S, Penn RD.. Cerebrospinal fluid flow in the normal and hydrocephalic human brain.. IEEE Trans Biomed Eng. 2007 Feb;54(2):291-302.

Zhang B, Li SB. Cine-PC MR in assessment of cerebrospinal fluid velocity in the aqueduct of the midbrain correlated with intracranial pressure--initial study.. Med Hypotheses. 2012 Feb;78(2):227-30. doi: 10.1016/j.mehy.2011.10.031. Epub 2011 Nov 17.

Question 287: Neuroimaging - Critical Care/Stroke

Discussion:

There is an ovoid area with decreased T2 along the anterior third ventricle, typical of a large flow void. The structure is also well seen as an irregular ovoid vascular structure arising from the anterior communicating artery typical of a saccular aneurysm.

References:

Atlas S. Magnetic resonance imaging of the brain and spine. 3rd ed. Philadelphia: Williams and Wilkins, 2002.

Question 289: Neuroimaging - Infection

Discussion:

The images demonstrate a multi-ring enhancing mass lesion within the left occipital lobe with marked adjacent vasogenic edema. The multi-ring masses have narrow, homogenously enhancing margins. There is marked increased diffusion signal within the masses. Marked increased signal on diffusion is more likely in an abscess as compared to a tumor. The extent of vasogenic edema and patterns of ring enhancement also would favor an infectious etiology. A subacute infarction can show luxury enhancement, which generally involves the cortical ribbon. The pattern of edema in an infarction is cytotoxic edema, not vasogenic as seen in this case. A cerebral abscess is the more likely consideration in this instance. The pathology confirmed Nocardia in this patient with diabetes.

References:

Atlas S. Magnetic resonance imaging of the brain and spine. 3rd ed. Philadelphia: Williams and Wilkins, 2002.

Question 290: Neuroimaging - Spine

Discussion:

There is a C2 vertebrae odontoid fracture. The clivus, C1 vertebrae lateral mass and posterior arch, and C2 spinous process appear normal.

References:

Pryputniewicz DM, Hadley MN. Axis Fractures. Neurosurgery 66:A68-A82, 2010

Question 291: Neuroimaging - Epilepsy

Discussion:

The images show clefts extending from the extra-axial space to the lateral ventricles bilaterally. These are most characteristic of open-lip schizencephaly. In porencephaly, the cyst is not lined by cortex, as it is here. In hydranencephaly there is little brain tissue around a central cyst. The appearance of encephalomalacia due to trauma is different, with areas of mixed signal intensity in frontal, temporal or occipital regions.

References:

Osborne A. Diagnostic imaging: brain. Philadelphia: Elsevier, 2004.

Question 292: Neuroimaging - Epilepsy

Discussion:

There is a complete absence of cortical sulci resulting in a smooth brain. This is the result of marked defect of neuronal migration and can occur either due to a genetic defect or acquired in utero on an infectious or ischemic basis. There are no clefts as would be seen with schizencephaly or heterotopia.

References:

A. James Barkovich and Charles Raybaud. Pediatric neuroimaging. 5th ed. Philadelphia: Lippincott, Williams & Wilkins, 2012.

Question 293: Neuroimaging - Infection

Discussion:

Toxoplasmosis is caused by an obligate intracellular parasite Toxoplasma gondii. Patients who develop AIDS are at particularly high risk of disseminated toxoplasmosis. T2 signal can vary from hypointense to hyperintense, and there is often considerable surrounding edema. The most common regions affected are the basal ganglia or thalami, followed by juxtacortical white matter.

References:

Greenberg JO, editor. Neuroimaging: a companion to Adams and Victor's principles of neurology. 2nd ed. New York: McGraw-Hill, 1999.

Question 296: Neuroimaging - Metabolic, Movement, CSF Circulatory Disorders

Discussion:

CADASIL (cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy) is characterized by a history of migraine headaches (30%-40% of individuals), mid-adult (30s-60s) onset of cerebrovascular disease progressing to dementia, and diffuse white matter lesions and subcortical infarcts on neuroimaging. The pathologic hallmark of CADASIL is electron-dense granules in the media of arterioles that can often be identified by electron microscopic (EM) evaluation of skin biopsies. More than 90% of individuals have mutations in NOTCH3, the only gene known to be associated with CADASIL. Molecular genetic testing is available on a clinical basis. The differential diagnosis of CADASIL includes multiple sclerosis (MS), sporadic small vessel disease including Binswanger disease, and primary angiitis of the nervous system [Williamson et al 1999]. The clinical characteristics and MRI abnormalities in these conditions may resemble those of CADASIL. The presence of temporopolar MRI lesions, the absence of optic nerve and spinal cord involvement, the absence of oligoclonal bands in the cerebrospinal fluid, and the absence of hypertension are critical in this regard [Dichgans et al 1999].

Other inherited disorders in the differential diagnosis include Fabry disease, CARASIL (cerebral autosomal recessive arteriopathy with subcortical infarcts and leukoencephalopathy) [Yanagawa et al 2002], MELAS (mitochondrial encephalomyopathy, lactic acidosis, and stroke-like episodes), and some forms of leukodystrophy. These disorders can be distinguished from CADASIL by the associated clinical signs, MRI, mode of inheritance, and appropriate laboratory investigations.

CADASIL should also be considered in any young person who has migraine with aura in conjunction with multiple white matter lesions on MRI [Gladstone & Dodick 2005].

From http://www.ncbi.nlm.nih.gov/bookshelf/br.fcgi?book=gene?=cadasil#cadasil.REF.auer.2001.443

References:

Auer DP, Putz B, Gossl C, Elbel G-K, Gasser T, Dichgans M. Differential Lesion Patterns in CADASIL and Sporadic Subcortical Arteriosclerotic Encephalopathy: MR Imaging Study with Statistical Parametric Group Comparison. Radiology 2001;218:443-451

Question 297: Neuroimaging - Critical Care/Stroke

Discussion:

Venous sinus thrombosis is diagnosed by the hyperdensity in the confluence of sinuses on head CT and by extensive T1-hyperintensity in the sagittal sinus and straight sinus on T1-weighted unenhanced MRI. There are no extra-axial hemorrhages or soft tissue swelling to suggest trauma. Aneurysmal bleeding typically causes subarachnoid hemorrhage. The findings are not seen in normal individuals.

References:

Choudhri, AF.. Pediatric neuroradiology. Thieme publishing, 2016..

Pathology

Question 4: Pathology - Toxic/Metabolic Disease

Discussion:

Methanol intoxication causes necrosis of the optic nerves and putamen. Neuronal loss in mammillary bodies is typical of Wernicke Korsakoff disease caused by thiamine deficiency. Neuronal loss in superior cerebellar vermis relates to mercury poisoning.

References:

Ellison DW, Love S. Neuropathology: A reference text of CNS pathology. 3rd ed. San Francisco: Elsevier, 2013.

Question 167: Pathology - Neuromuscular Disease

Discussion:

Target fibers, which are best seen with Masson trichrome or NADH stains, are characteristic of denervation/ reinnervation. Central cores are similar in appearance but extend the length of the fiber and are seen as a form of congenital myopathy. Polymyositis or myasthenia gravis do not typically show target fibers in the range of pathological findings.

References:

Dubowitz V. Muscle Biopsy: a practical approach. 4th ed. Saunders, 2013. pp. 346-351.

Question 191: Pathology - Cerebrovascular Disease

Discussion:

Intimal fibroplasia is the major histopathological finding in the vessels in moyamoya syndrome. Neither complicated atherosclerotic plaques nor vasculitis are histological features. PAS-positive granules are seen in cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL).

References:

Love S, Louis DN, Ellison D. Greenfield's neuropathology. London: Hodder Arnold, 2008.

Love, S., Budka,H.,Ironside, J.W., and Perry, A.. Greenfield's Neuropathology. 9th edition, Boca Raton, FL: CRC Press, 2015

Question 201: Pathology - Infectious Disease

Discussion:

The pathologic images show neurocysticercosis caused by the pork tapeworm, Taenia solium. In the H&E images, the wall of a cysticercus is identified and these form cystic structures as shown. The wall of the cysticercus contains a densely eosinophilic cuticular layer, a middle cellular layer, and a loose stromal layer containing excretory channels. In the racemose form of neurocysticercosis, only these cystic forms of the organism are identified and there is not a scolex, as seen in intraparenchymal lesions. Dermoid, neuroenteric, and Rathke cleft cysts would have epithelial linings comprising squamous cells (Dermoid), respiratory-type or gastrointestinal-type epithelia (Neurenteric cyst), and ciliated epithelium (Rathke cleft cyst). In addition, aside from dermoid cyst of the cerebellopontine angle, the anatomic location is not correct for these other benign, cystic lesions. Metastases may be cystic, but these would also have a malignant epithelium lining resembling the primary site, as well as nuclear pleomorphic and mitotic activity.

References:

Love, S., Budka,H.,Ironside, J.W., and Perry, A.. Greenfield's Neuropathology. 9th edition, Boca Raton, FL: CRC Press, 2015

Question 205: Pathology - Cerebrovascular Disease

Discussion:

The photographs show a cavernous malformation, not the hemangioblastoma of von Hippel-Lindau disease or the superficial angiomatosis of Sturge-Weber disease. CREST syndrome (calcinosis, Raynaud, esophageal motility disorders, sclerodactyly, telangiectasia) does not have CNS manifestations. Familial amyloidosis usually affects peripheral nerves; most cerebral amyloid angiopathy is sporadic and not familial with the exception of Dutch, Icelandic, and British variants.

Patients with autosomal dominant cerebral cavernous malformation syndrome may have mutations of the KRIT1 gene on chromosome 7q. Other familial cases have been linked to genes on chromosomes 7p and 3q.

References:

Ellison DW, Love S. Neuropathology: A reference text of CNS pathology. 3rd ed. San Francisco: Elsevier, 2013.

Question 217: Pathology - Neurodegenerative Disease

Discussion:

Hippocampal sclerosis of aging (HS-Aging) is the best diagnosis for this patient with a late-onset amnestic syndrome, bilateral hippocampal atrophy and massive neuronal loss limited to hippocampus, and with TDP-43 neuronal inclusions in limbic structures including dentate gyrus. HS-Aging is a common disorder of the “oldest old” in the US population (patients > 85 years) and may be mistaken clinically for mild Alzheimer’s disease. However, the absence of tau and amyloid pathologies, as well as the absence of more global cerebral atrophy, excludes a diagnosis of Alzheimer’s disease. Likewise, the absence of synuclein pathology excludes dementia with Lewy bodies. The absence of more extensive TDP-43 pathology in neocortex and the absence of more global atrophy excludes an FTLD-TDP. Finally, Pick’s disease is a subtype of FTLD-tau and would have extensive tau pathology with characteristic tau-immunoreactive Pick bodies, including in the dentate gyrus (not identified in this patient).

References:

Love, S., Budka,H.,Ironside, J.W., and Perry, A.. Greenfield's Neuropathology. 9th edition, Boca Raton, FL: CRC Press, 2015

Dickson D, Weller RO. Neurodegeneration: the molecular pathology of dementia and movement disorders. 2nd ed. West Sussex, UK: Wiley-Blackwell, 2011

Question 218: Pathology - Neuromuscular Disease

Discussion:

The muscle biopsy specimen shows a necrotizing vasculitis with fibrinoid necrosis of the vessel walls, not amyloid angiopathy. Vasculitis may be seen in amphetamine-induced vasculitis, polyarteritis nodosa, rheumatoid vasculitis, and granulomatosis with polyangiitis (Wegener’s granulomatosis). Takayasu arteritis affects large blood vessels such as aortic arch, not small intramuscular vessels. Inclusion body myositis is an inflammatory myopathy with rimmed vacuoles, not a vasculitis.

References:

Dubowitz V. Muscle Biopsy: a practical approach. 4th ed. Saunders, 2013. pp. 346-351.

Engel AG, Franzini-Armstrong C. Myology. 3rd ed. New York: McGraw-Hill, 2004.

Alan Pestronk, MD, website author. Neuromuscular Disease Center. Available from:
http://www.neuro.wustl.edu/NEUROMUSCULAR/antibody/pnimax.html#pan [Accessed March 2010].
http://www.neuro.wustl.edu/NEUROMUSCULAR/time/nmacute.htm#neuropathy [Accessed March 2010].

Question 231: Pathology - Tumors

Discussion:

Hemangioblastoma is a highly vascular tumor that most often arises in the cerebellar hemisphere, but that may also arise within the spinal cord and rarely in supratentorial locations. Histopathologic examination of these tumors shows variably sized vascular channels and numerous capillaries, as well as stromal tumor cells that have vacuolated ("foamy") cytoplasm. The stromal cells contain lipid, which may be highlighted by Oil Red O stain on frozen section material, as shown in the images. Nuclei may be very pleomorphic, which represents a degenerative change rather than a feature of malignancy. von Hippel Lindau (vHL) disease, due to mutations in the VHL gene, should be considered in any patient with hemangioblastoma. However, in the majority of patients the tumor arises sporadically.

References:

Perry A, Brat DJ. Practical surgical neuropathology: a diagnostic approach. Philadelphia: Churchill Livingstone Elsevier, 2010.

Louis DN, Ohgaki H, Wiestler OD, Cavenee WK, Ellison, DW, Fiarella-Branger D, Perry A, Reifenberger G, von Deimling A. WHO classification of tumours of the central nervous system. 5th ed. Lyon: International Agency for Research on Cancer, 2016.

Question 233: Pathology - Cerebrovascular Disease

Discussion:

Porencephaly is felt to be a milder form of hydranencephaly which is theorized to be secondary to a vascular insult during gestation. Both arise in the middle cerebral artery or larger (internal carotid) distribution. Symptoms may include spastic paraplegia, seizures and/or developmental delays. The lesions are most often smooth-walled with frequent associated abnormal gyral patterns, including heterotopias. Typically they are full-thickness from surface of the brain to the ventricle, and are frequently bilateral.

References:

Burger, Scheithauer, Kleinschmidt-DeMasters, Rodriguez, Tihan. Neuropathology. 2nd ed. Salt Lake City Utah: Elsevier, 2016.

Question 234: Pathology - Demyelinating Disease

Discussion:

The clinical features, coupled with the perivenular inflammatory and demyelinating features illustrated in the images on the Luxol fast blue/periodic acid-Schiff stain for myelin (LFB/PAS in which the LFB is the portion of the stain specific for myelin), are pathognomonic for acute disseminated encephalomyelitis. The disease usually affects children and young adults, presents abruptly with headaches and fever usually 2 to 12 days after an infection, and resolves rapidly within a week. Usually, there are no residual neurologic deficits, and most cases are now nonfatal. Historically, this monophasic acute demyelinating disorder was associated with smallpox vaccinations and then later was identified after measles, mumps, rubella, varicella, or vaccinia infections. Today, usually the disorder follows a nonspecific upper respiratory illness.

References:

Love, S., Budka,H.,Ironside, J.W., and Perry, A.. Greenfield's Neuropathology. 9th edition, Boca Raton, FL: CRC Press, 2015

Ellison D, Love S, Chimelli L, et al. Neuropathology. A reference text of CNS pathology. 3rd ed. Edinburgh: Elsevier Mosby, 2013

Question 240: Pathology - Epilepsy

Discussion:

Focal cortical dysplasia type II b is characterized by balloon cells and dysmorphic neurons. Balloon cells have a large amount of glassy eosinophilic cytoplasm lacking Nissl substance. Multiple nuclei are often present in these cells. They may be seen in groups. Dysmorphic neurons are enlarged with large nuclei and abnormally distributed Nissl substance. They are often maloriented. Dysmorphic neurons are not in DNTs, globoid cell leukodystrophy, hippocampal sclerosis, or PXAs. DNTs contain normal-appearing neurons with mucin pools and oligodendroglial-like cells. PXAs are glial tumors with variably pleomorphic nuclei or bubbly cytoplasm. Globoid cells are actually large multinucleated macrophages, there is depletion of neurons in hippocampal sclerosis with a concomitant gliosis.

References:

Burger, Scheithauer, Kleinschmidt-DeMasters, Rodriguez, Tihan. Neuropathology. 2nd ed. Salt Lake City Utah: Elsevier, 2016.

Question 241: Pathology - Basic Reactions

Discussion:

Muscle spindles are structures within the connective tissue capsule of skeletal muscle consisting of striated, intrafusal fibers of varying number and size. The spindle acts as a sensory organ for muscle stretch. It is important not to mistake these fibers as diseased extrafusal muscle fibers.

References:

Dubowitz V. Muscle Biopsy: a practical approach. 4th ed. Saunders, 2013. pp. 346-351.

Question 244: Pathology - Tumors

Discussion:

The periventricular lesion is a subependymal giant cell astrocytoma (SEGA). The patient has tuberous sclerosis (TS). Patients with tuberous sclerosis have tubers, SEGAs, rhabdomyomas, angiomyolipomas, lymphangioleiomyomatosis, adenoma sebaceum (angiofibromas), and other skin findings.

References:

Burger, Scheithauer, Kleinschmidt-DeMasters, Rodriguez, Tihan. Neuropathology. 2nd ed. Salt Lake City Utah: Elsevier, 2016.

Question 247: Pathology - Infectious Disease

Discussion:

The pathologic images show a multinucleated giant cell in the setting of granulomatous inflammation. In addition, the H&E image shows a fungal organism in the multinucleated giant cell and the GMS stain, used to identify fungal organisms, shows a thick-walled spherule containing multiple, small endospores, diagnostic of Coccidioides. If performed, fungal cultures of the specimen will most likely confirm this as Coccidioides immitis. When it involves the nervous system, Coccidioides frequently involves the leptomeninges and leads to a basilar leptomeningitis with mental status changes, as in this patient. Granulomatous meningitis may also be caused by neurosarcoidosis, some forms of amebic meningoencephalitis, and mycobacteria. However, the fungal elements on GMS stain exclude these other possible diagnoses.

References:

Love, S., Budka,H.,Ironside, J.W., and Perry, A.. Greenfield's Neuropathology. 9th edition, Boca Raton, FL: CRC Press, 2015

Question 256: Pathology - Toxic/Metabolic Disease

Discussion:

Wernicke encephalopathy classically presents with a triad of confusion, ataxia, and nystagmus, but many patients do not manifest the entire triad clinically. Wernicke encephalopathy after obesity surgery has been recently recognized as an important complication and usually occurs 4 to 12 weeks postoperatively, especially in young women with vomiting.

References:

Love, S., Budka,H.,Ironside, J.W., and Perry, A.. Greenfield's Neuropathology. 9th edition, Boca Raton, FL: CRC Press, 2015

Singh S, Kumar A. Wernicke encephalopathy after obesity surgery: a systematic review. Neurology 2007;68:807-811.

Question 261: Pathology - Neurodegenerative Disease

Discussion:

The image shows severe pontine atrophy and would most likely be seen in the olivopontocerebellar atrophy (OPCA) form of multiple system atrophy (MSA). In multiple system atrophy, glia (especially oligodendroglia) exhibit cytoplasmic, flame-shaped, silver-positive inclusions that are also immunoreactive for p62, ubiquitin and alpha-synuclein.

References:

Dickson D, Weller RO. Neurodegeneration: the molecular pathology of dementia and movement disorders. 2nd ed. West Sussex, UK: Wiley-Blackwell, 2011

Ellison DW, Love S. Neuropathology: A reference text of CNS pathology. 3rd ed. San Francisco: Elsevier, 2013.

Question 263: Pathology - Infectious Disease

Discussion:

Rabies is endemic in animals in the Americas, Europe, Africa, and Central Asia. Rabies is usually transmitted by the bite of a rabid animal, but rare examples of aerosol transmission are recognized. The prodrome includes flulike symptoms and occasionally pain or paresthesias at the site of the bite. Furious rabies (symptoms outlined in this history) is the more common form. The classic histologic feature (shown in the image) is the Negri body, which is a round or oval eosinophilic inclusion in the cytoplasm of neurons (easiest to find in the Purkinje cells and hippocampal pyramidal cells).

References:

Ellison DW, Love S. Neuropathology: A reference text of CNS pathology. 3rd ed. San Francisco: Elsevier, 2013.

Question 268: Pathology - Toxic/Metabolic Disease

Discussion:

Central pontine myelinolysis (CPM) has been most closely associated with the too-rapid correction of profound hyponatremia. It has been described in a variety of patients including alcoholics with Wernicke-Korsakoff syndrome, but many non-alcoholic patient groups have also been reported. The latter include liver transplant recipients and patients with severe burns, malnutrition, severe electrolyte disorders, and anorexia. Hypophosphatemia, but not thyroid disorders or hypoglycemia, has also been postulated to be related to CPM.

References:

Kleinschmidt-DeMasters BK, Rojiani AM, Filley C. Central and extrapontine myelinolysis: then and now. J Neuropathology Exp Neurol 2006;65:1-11.

Ellison DW, Love S. Neuropathology: A reference text of CNS pathology. 3rd ed. San Francisco: Elsevier, 2013.

Question 270: Pathology - Critical Care/Stroke

Discussion:

The photograph shows remote bilateral frontal and left temporal contusions with a slight orange tinge secondary to the presence of residual hemosiderin-laden macrophages. The olfactory nerves are disrupted, which undoubtedly would have led to anosmia.

References:

Ellison DW, Love S. Neuropathology: A reference text of CNS pathology. 3rd ed. San Francisco: Elsevier, 2013.

Question 273: Pathology - Developmental

Discussion:

The image illustrates a smooth brain, showing sulcal development compatible with a normal 24-week gestational aged fetus, with an open insula and development of the Rolandic fissure as visible in this lateral view. The cerebellum is normally smaller in proportion to the sizes of the hemispheres in the immature brain. Lissencephaly is the term that applies to a more mature brain with a smooth surface related to deficient neuronal migration. There are no gross features to suggest holoprosencephaly or polymicrogyria.

References:

Ellison DW, Love S. Neuropathology: A reference text of CNS pathology. 3rd ed. San Francisco: Elsevier, 2013.

Question 275: Pathology - Tumors

Discussion:

The image shows a colloid cyst of the third ventricle. Patients can occasionally manifest sudden death from this otherwise histologically benign lesion. Hypothalamic hamartoma would be within the hypothalamus, not the third ventricle. Lipomas classically are seen near the corpus callosum. Subependymomas only occur rarely in the third ventricle.

References:

Prayson RA. Neuropathology. 2nd ed. Philadelphia: Elsevier, 2012.

Question 276: Pathology - Neurodegenerative Disease

Discussion:

Corticobasal degeneration (CBD) is a 4-repeat tauopathy characterized by tau-immunoreactive lesions, and in particular, numerous tau-positive threads in cerebral white matter and white matter of subcortical nuclei. In addition, glial pathology is common, including astrocytic plaques, comprising tau-immunoreactive astrocytic processes. Tau pathology may also be abundant in brainstem and cerebellum and may overlap with pathologic findings in progressive supranuclear palsy (PSP). As in this vignette, not all CBD patients will present with characteristic symptoms of the corticobasal syndrome and patients may also present with executive dysfunction and aphasia. The innumerable tau-immunoreactive threads in white matter, as shown in the image, would not be expected in the other neurodegenerative syndromes listed.

References:

Dickson D, Weller RO. Neurodegeneration: the molecular pathology of dementia and movement disorders. 2nd ed. West Sussex, UK: Wiley-Blackwell, 2011

Question 284: Pathology - Hypothalamus/Pituitary

Discussion:

The diagnosis of neurosarcoidosis is often difficult in life due to its protean manifestations. Usually symptoms referable to cranial nerve or meningeal involvement predominate, although in this woman spinal cord symptoms and myelopathy were her first presentation. The most common systemic organ involvement is in lung. Skeletal muscle and peripheral nerve are often also involved. Cardiac muscle involvement is less common than lung. Sarcoid is a diagnosis of exclusion, and most specific serological testing is negative. Hypercalcemia, if present, is sometimes helpful in pointing toward the diagnosis of sarcoidosis.

References:

Ellison D, Love S, Chimelli L, et al. Neuropathology. A reference text of CNS pathology. 3rd ed. Edinburgh: Elsevier Mosby, 2013

Joseph FG, Scolding NJ. Sarcoidosis of the nervous system. Pract Neurol 2007;7:234?244.

Question 294: Pathology - Cerebrovascular Disease

Discussion:

The graphic illustrates bilateral, nearly symmetric, parasagittal, cortical and basal ganglia venous infarctions due to thrombosis of the superior sagittal sinus and deep cerebral veins.

References:

Ellison DW, Love S. Neuropathology: A reference text of CNS pathology. 3rd ed. San Francisco: Elsevier, 2013.

Question 389: Pathology - Neuromuscular Disease

Discussion:

Inclusion body myositis has pathologic features of an inflammatory myopathy, but in addition has features of impaired autophagy, as demonstrated by rimmed vacuoles in muscle cells containing autophagic debris. The accumulation of pathologic proteins, including the autophagy pathway-related protein 62, phosphorylated TDP-43 and phosphorylated tau is also characteristic. In addition, biopsy specimens may show features of neurogenic atrophy and abnormalities on oxidative enzyme stains (e.g., COX-negative fibers). Muscular dystrophies in general do not tend to have a significant inflammatory component. Neurogenic atrophic presents in muscle as esterase-positive angulated atrophic fibers. Polymyositis, while a form of inflammatory myopathy, does not contain rimmed vacuoles or autophagic debris. Steroid myopathy is typified by a type 2 fiber specific atrophy.

References:

Dubowitz V, Sewry CA. Muscle biopsy; a practical approach. 3rd ed. Philadelphia: Saunders, Elsevier, 2007.

Pharmacology/Chemistry

Question 14: Pharmacology/Chemistry - Cerebrovascular Disease

Discussion:

Clopidogrel is converted to its active metabolite by cytochrome P450 (CYP). Individuals with genetic variants of CYP are poor metabolizers of clopidogrel and may not develop adequate anti-platelet aggregation with therapeutic dosing, thus resulting in reduced drug efficacy. The FDA has placed a black box warning on the clopidogrel label as a consequence of this finding. Medications which inhibit CYP, such as omeprazole, may also reduce efficacy of clopidogrel.

References:

Hulot JS, Collet JP, Silvain J, et al. Cardiovascular risk in clopidogrel-treated patients according to cytochrome P450 2C19*2 loss-of-function allele or proton pump inhibitor coadministration: a systematic meta-analysis. J Am Coll Cardiol 2010;56(2):134-143.

Question 16: Pharmacology/Chemistry - Other Pain Syndromes

Discussion:

Pregabalin was approved in 2007 by the US Food and Drug Administration (FDA) as the first drug for the treatment of fibromyalgia, effective in reducing symptoms of pain, disturbed sleep and fatigue. Pregabalin had been approved earlier by the FDA for the treatment of neuropathic pain associated with diabetic peripheral neuropathy, postherpetic neuralgia, and as adjunctive therapy for refractory partial seizures. Pregabalin also has proven efficacy in adjunctive therapy of generalized anxiety disorder, social anxiety disorder, and acute pain. It has been demonstrated that although pregabalin is a structural derivative of the inhibitory neurotransmitter GABA, it does not bind directly to GABAA, GABAB, or benzodiazepine receptors; it does not augment GABAA responses in vitro, nor does it alter GABA concentration in the animal brain or have acute effects on GABA

uptake or degradation. Pregabalin does not block sodium channels, is not active at opiate receptors, and does not alter cyclooxygenase enzyme activity. It is inactive at serotonin and dopamine receptors and does not inhibit dopamine, serotonin, or noradrenaline reuptake.

However, a single common mechanism, inhibition of calcium currents via high-voltage-activated channels containing the alpha2delta-1 subunit, leading in turn to reduced neurotransmitter release and attenuation of postsynaptic excitability, is believed to have a predominate effect on its mechanism of action.

References:

Zareba G. New treatment options in the management of fibromyalgia: role of pregabalin. Neuropsychiatr Dis Treat 2008;4:1193-1201.

Sills GJ. The mechanisms of action of gabapentin and pregabalin. Curr Opin Pharmacol 2006;6:108-113.

Question 25: Pharmacology/Chemistry - Movement Disorders

Discussion:

All direct acting dopamine agonists in clinical use for Parkinson disease – including ropinirole, pramipexole, cabergoline and pergolide, have been shown to have a dramatically reduced incidence of dyskinesias, compared to levodopa. However, there is a clear increased incidence of hallucinations, peripheral edema and compulsive behaviors. There is no good evidence for a difference in the rate of neurodegeneration

References:

Antonini A, Tolosa E, Mizuno Y, Yamamoto M, Poewe WH.. A reassessment of risks and benefits of dopamine agonists in Parkinson's disease.. Lancet Neurol. 2009 Oct;8(10):929-37.

Jenner P.. Preventing and controlling dyskinesia in Parkinson's disease--a view of current knowledge and future opportunities.. Mov Disord. 2008;23 Suppl 3:S585-98.

Question 32: Pharmacology/Chemistry - Epilepsy

Discussion:

The increased risk of bone disease in patients with epilepsy manifests as a 1.3 to 3.8 relative risk of osteopenia (diagnosed with dual energy x-ray absorptiometry [DEXA] scanning as a T-score of -1 to -2.5), a 1.7 to 3.8 relative risk of osteoporosis (defined as a T-score on DEXA scanning of less than -2.5), and a 1.7 to 6.1 relative risk of fractures. Several AEDs have been linked with bone disease. These mostly include cytochrome P450 enzyme inducers, such as phenytoin, phenobarbital, primidone, and carbamazepine. Multiple studies associated EIAEDs with markers of a disturbed vitamin D-parathyroid hormone axis, such as higher bone turnover, reduced serum concentration of vitamin D, and reduced bone mineral density. A documented link between valproate (an AED that actually inhibits cytochrome P450) and increased serum concentration of calcium with decreased serum levels of vitamin D metabolites suggests additional mechanisms for impaired bone health with AED use beyond a P450 system induction. A few studies evaluating the newer AEDs lamotrigine, gabapentin, topiramate, and tiagabine found no evidence of impaired bone health with these medications.

References:

Carlson C; Anderson CT.. Special Issues in Epilepsy: The Elderly, the Immunocompromised, and Bone Health.. CONTINUUM: Lifelong Learning in Neurology. 22(1 Epilepsy):246-61, 2016 Feb.

Question 33: Pharmacology/Chemistry - Epilepsy

Discussion:

Lethargy, irritability, and anorexia are common symptoms in patients with hyperammonemia. Disorders of urea cycle are common in developmentally delayed patients with epilepsy. VPA increases levels of gamma-aminobutyric acid and prolongs the recovery of inactivated sodium channels. These properties may be responsible for its action as a CNS depressant. VPA may also

cause impairments in fatty-acid metabolism and disrupt the urea cycle, leading to hyperammonemia. VPA also alters fatty-acid metabolism, impairs beta-oxidation (a mitochondrial process), and disrupts the urea cycle. Hyperammonemia and other metabolic effects, as well as end-organ effects (hepatitis, pancreatitis, hemodynamic compromise), may be the result of severe toxicity due to these impaired metabolic processes.

There are no known drug-drug interactions between valproate and levetiracetam. No reports of levetiracetam-induced hepatitis are in the literature.

References:

Lamictal (Lamotrigine) Drug Information. 2013. Available from http://www.rxlist.com/lamictal-drug/side-effects-interactions.htm

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Question 43: Pharmacology/Chemistry - Demyelinating Disorders

Discussion:

Contraception is generally recommended to prevent teratogenicity for women with MS taking disease-modifying agents. However, teratogenicity due to involvement of male sperm has been observed with teriflunomide. Male patients with MS should be counseled on their reproductive plans before initiating treatment with teriflunomide.

References:

The American Academy of Neurology. Practice Guideline: Disease-modifying therapies for adults with multiple sclerosis. Neurology online 2018

Cree BA.. Update on reproductive safety of current and emerging disease-modifying therapies for multiple sclerosis.. Mult Scler 2013;19:835-43.

Question 44: Pharmacology/Chemistry - Movement Disorders

Discussion:

Dopamine agonist treatment in Parkinson disease has been associated with several impulse control disorders, including pathologic gambling, hypersexuality, compulsive eating, and compulsive shopping.

References:

Gschwandtner U, Aston J, Renaud S, Fuhr P. Pathologic gambling in patients with Parkinson's disease. Clin Neuropharmacol 2001;24:170-172.

Olanow CW, Stern MB, Sethi K. The scientific and clinical basis for the treatment of Parkinson disease. Neurology 2009;72 (Suppl 4):S1-S136.

Question 51: Pharmacology/Chemistry - Cerebrovascular Disease

Discussion:

This patient had a transient ischemic attack (TIA). Her TIA would be considered moderate-risk with an ABCD2 score of 5, which gives her about a 10% risk of ischemic stroke within 90 days. The POINT trial (Clopidogrel and Aspirin in Acute Ischemic Stroke and High-Risk TIA) studied secondary stroke prevention in patients with a minor acute ischemic stroke with an NIH stroke scale score of 3 or less) or a high-risk TIA with a score of 4 or more on the ABCD2 scale. In this population, the combination of clopidogrel and aspirin for 90 days reduced the rate of major ischemic to 5.0% compared to 6.5% in patients receiving aspirin plus placebo (hazard ratio, 0.75; 95% confidence interval [CI], 0.59 to 0.95; P=0.02), with most events occurring during the first week after the initial event. Major hemorrhage occurred in 23 patients (0.9%) receiving clopidogrel plus aspirin and in 10 patients (0.4%) receiving aspirin plus placebo. The POINT trial is concordant with the CHANCE trial in China, which also showed a benefit for dual antiplatelet therapy for 90 days in patients with minor stroke or transient ischemic attack. While dual antiplatelet therapy for 90 days after minor ischemic stroke or high-risk TIA has shown additional benefit in secondary stroke prevention beyond the rate of increased hemorrhage, triple anti-platelet therapy with clopidogrel, aspirin and

dipyridamole was studied in the TARDIS trial. This study was discontinued early as there was no significant difference in the rate of ischemic stroke but there was a increased risk of hemorrhagic complications (adjusted cOR 254, 95% CI 205?316, p<00001).

References:

Philip M Bath, Lisa J Woodhouse, Jason P Appleton, et al. Antiplatelet therapy with aspirin, clopidogrel, and dipyridamole versus clopidogrel alone or aspirin and dipyridamole in patients with acute cerebral ischaemia (TARDIS). Lancet Vol 391 March 3, 2018

S. Claiborne Johnston, M.D., Ph.D., J. Donald Easton, M.D., Mary Farrant, M.B.A., et al. Clopidogrel and Aspirin in Acute Ischemic Stroke and High-Risk TIA. New England Journal of Medicine, May 16, 2018

Wang YO, Wang YI, Zhao X, Liu L, Wang D, et al. Clopidogrel with Aspirin in Acute Minor Stroke or Transient Ischemic Attack. N Engl J Med; 2013; 369:11-19

Question 54: Pharmacology/Chemistry - Movement Disorders

Discussion:

Progressive supranuclear palsy (PSP), corticobasal degeneration (CBD) and frontotemporal dementia with parkinsonism (FTDP) have all been associated with abnormalities in the structures of tau proteins - either mutations with altered amino acid incorporation or hyperphosphorylation. Beta-amyloid and presenilin mutations are seen in some of the young-onset familial Alzheimer disease. Orexin is depleted, but not modified in narcolepsy.

References:

Ludolpha AC, Kassubeka J, Landwehrmeyer BG, et al. Tauopathies with parkinsonism: clinical spectrum, neuropathologic basis, biological markers, and treatment options. European Journal of Neurology 2009, 16: 297?309

Question 57: Pharmacology/Chemistry - Dementia

Discussion:

This patient has clinical features and findings of early probable Alzheimer disease (AD), characterized by progressive short-term memory impairment and cognitive dysfunction in multiple domains (language, visuospatial, and executive). Definite AD requires the demonstration of pathologic hallmarks on autopsy: global neuronal atrophy and loss of synapses, deposition of extracellular amyloid protein (A-beta 1-42), and accumulations of intracellular neurofibrillary tangles (NFT). NFTs are composed of paired filaments of phosphorylated tau protein. Clinical progression of dementia in AD correlates with NFT tissue burden. Studies of CSF in AD have shown significantly decreased levels of A beta 1-42 and elevated levels of tau and phosphorylated-tau compared with age-matched controls. However, these changes are not specific for AD, and can be found in individuals with other neurodegenerative disorders and in normal aging. Thus, the utility of CSF testing in the evaluation of AD and dementia is unsettled. Cognitive symptoms of AD in patients include centrally-acting cholinesterase inhibitors (donepezil, rivastigmine, galantamine) and the NMDA-antagonist memantine.

References:

Farlow MR. Alzheimer disease. Continuum Lifelong Learning Neurol 2007;13(2):39-68.

De Meyer, G, Shapiro F, Vanderstichele H et al.. Diagnosis-Independent Alzheimer Disease Biomarker Signature in Cognitively Normal Elderly People. Arch Neurol. 2010;67(8):949-956.

Question 64: Pharmacology/Chemistry - Epilepsy

Discussion:

The most recent combined estrogen and progestin contraceptive pills contain only 20?35 mg of ethinyl estradiol (EE). The dose of EE in these agents is too low to ensure suppression of ovulation and serves mainly to provide proper cycle control, whereas the progestin component is responsible for the contraceptive mechanisms which include inhibition of ovulation as well as increased

viscosity of the cervical mucus and reduced endometrial suitability for ovum implantation. Carbamazepine, phenobarbital, and phenytoin are potent enzyme inducers and can accelerate the metabolism of hormonal contraceptives, thus increasing the risk of unplanned pregnancy. Oxcarbazepine also has a lower potential to enzyme induction, but unfortunately exerts a similar effect on hormonal contraceptives as carbamazepine [34]. Eslicarbazepine is the S-enantiomer of the active constituent of oxcarbazepine and does also reduce the plasma concentrations of EE and progestins. A selective, dose dependent induction of progestin metabolism has been demonstrated for perampanel, an effect thought to be clinically significant at 12 mg. Available data, although sparse, suggest that neither valproate, gabapentin, levetiraceta, zonisamide, nor lacosamide affect the metabolism of combined estrogen and progestin contraceptive pills. Lamotrigine, however, may have a modest decreasing effect on the plasma level of the levonorgestrel while the EE compound is not affected.

References:

Reimers A; Brodtkorb E; Sabers A.. Interactions between hormonal contraception and antiepileptic drugs: Clinical and mechanistic considerations. Seizure. 28:66-70, 2015 May.

Question 65: Pharmacology/Chemistry - Aging, Degenerative Diseases

Discussion:

In 9/12, florbetapir (Amyvid) was approved by the FDA for the imaging of beta-amyloid protein aggregates in the brain. These aggregates form the core of neuritic plaques, one of the two pathological hallmarks of Alzheimer's disease. The other pathological hallmark of Alzheimer disease is neurofibrillary tangles composed of phosphorylated tau proteins. Pittsburgh compound B is also approved for the imaging of beta-amyloid protein aggregates in the brain but is less available for routine clinical use due to its short half-life.

References:

Lucie Yang, M.D., Ph.D., Dwaine Rieves, M.D., and Charles Ganley, M.D.. Brain amyloid imaging--FDA approval of florbetapir F18 injection.. New England Journal of Medicine; 2012; 367(10):885-7

Question 74: Pharmacology/Chemistry - Movement Disorders

Discussion:

In a randomized controlled multicenter trial study, 117 patients with moderate to severe tardive dyskinesia received deutetrabenazine or placebo. For the primary endpoint, deutetrabenazine significantly reduced Abnormal Involuntary Movement Scale scores from baseline to week 12 vs placebo -3.0 [0.45] vs -1.6 [0.46], p = 0.019). In addition, no worsening in parkinsonism, as measured by the Unified Parkinson's Disease Rating Scale motor subscale, was noted from baseline to week 12 in either group. In a small randomized controlled study of 22 patients with tardive dyskinesia, amantadine reduced abnormal involuntary movements greater than placebo. Olanzapine, trihexyphenidyl may produce or worsen tardive dyskinesia. Sertraline has not shown any effect on tardive dyskinesia. In a small randomized controlled study of 33 patients, selegiline was worse than placebo in improving involuntary movements.

References:

Goff DC1, Renshaw PF, Sarid-Segal O, Dreyfuss DA, Amico ET, Ciraulo DA.. A placebo-controlled trial of selegiline (L-deprenyl) in the treatment of tardive dyskinesia. Biol Psychiatry. 1993 15;33(10):700-6.

Pappa S1, Tsouli S, Apostolou G, Mavreas V, Konitsiotis S.. Effects of amantadine on tardive dyskinesia: a randomized, double-blind, placebo-controlled study. Clin Neuropharmacol 2010, 33(6):271-5.

Fernandez HH; Factor SA; Hauser RA; Jimenez-Shahed J; Ondo WG; Jarskog LF; Meltzer HY; Woods SW; Bega D; LeDoux MS; Shprecher DR; Davis C; Davis MD; Stamler D; Anderson KE.. Randomized controlled trial of deutetrabenazine for tardive dyskinesia: The ARM-TD study.. Neurology. 88(21):2003-2010, 2017 May 23.

Question 76: Pharmacology/Chemistry - Headache

Discussion:

Medical therapy with carbonic anhydrase inhibitor (acetazolamide or topiramate) is utilized for patients with idiopathic increased intracranial pressure with surgical intervention usually considered when visual loss is threatened. Nephrolithiasis, although uncommon, is a known complication among carbonic anhydrase inhibitor and usually develops within the first year and a half after treatment initiation. Furosemide is usually an alternative or an add-on in case the use of carbonic anhydrase inhibitor is not appropriate or not sufficient.

References:

Au JN, Waslo CS, McGwin G, et al.. Acetazolamide-induced nephrolithiasis in idiopathic intracranial hypertension patients. J Neuroophthalmol 2016;36(2):126-30.

Question 79: Pharmacology/Chemistry - Demyelinating Disorders

Discussion:

Natalizumab (Tysabri) is a recombinant humanized monoclonal antibody that binds to alpha4beta1-integrin that is expressed on activated T-lymphocytes. By blocking the interaction of alpha4beta1--integrin with the vascular cell adhesion molecule 1 (VCAM-1) ligand on endothelial cells, natalizumab inhibits adhesion and transmigration of activated T-lymphocytes across the blood-brain barrier, reducing CNS inflammation in MS. In February 2005, 3 months after natalizumab (NTZ) first received FDA approval for treatment of relapsing-remitting multiple sclerosis (RRMS), the drug was withdrawn from the market when 3 cases of progressive multifocal leukoencephalopathy (PML) were reported in natalizumab-treated patients who participated in clinical trials in MS and Crohn disease. PML is a typically fatal opportunistic infection of central nervous system oligodendrocytes caused by reactivation of latent JC polyomavirus infection. It is primarily seen in disorders associated with severely impaired cell-mediated immunity, including acquired immunodeficiency syndrome (AIDS), leukemia, and organ transplantation. After infection in immunocompetent hosts, the JC virus remains quiescent in kidney tissue and is often detected in urine. CNS infection is likely established via hematogenous dissemination of virus across the blood-brain barrier. It is plausible that inhibition of leukocyte trafficking into the CNS by natalizumab is responsible in part for PML. Risk factors for natalizumab-associated PML include positive serum JCV antibody, duration of therapy over 2 years, and prior history of immunosuppression. The risk of PML with all of these risk factors is 1:90.

There is no treatment established for PML. Current recommendations for NTZ-associated PML include stopping the medication and then initiating plasma exchange to remove the drug from the circulation. Restoration of immune function may result in immune reconstitution inflammatory syndrome (IRIS), with worsening neurologic symptoms. Most experts recommend treating IRIS with pulse high-dose intravenous steroids, sometimes followed by oral steroids. Duration of treatment is not established and is determined on a case-by-case basis.

References:

Srensen PS1, Bertolotto A, Edan G, Giovannoni G, Gold R, Havrdova E, Kappos L, Kieseier BC, Montalban X, Olsson T.. Risk stratification for progressive multifocal leukoencephalopathy in patients treated with natalizumab.. Mult Scler. 2012 Feb;18(2):143-52

Goodin DS, Cohen BA, O'Connor P, Kappos L, Stevens JC. Assessment: The use of natalizumab (Tysabri) for the treatment of multiple sclerosis (an evidence-based review): Report of the Therapeutics and Technology Assessment Subcommittee. of the American Academy of Neurology. Neurology 2008;71(10):766-773.

Khatri BO, Man S, Giovannoni G, et al. Effect of plasma exchange in accelerating natalizumab clearance and restoring leukocyte function. Neurology 2009;72:402-409.

Gold R, Jawad A, Miller DH, et al. Expert opinion: guidelines for the use of natalizumab in multiple sclerosis patients previously treated with immunomodulating therapies. J Neuroimmunol 2007;187:156-158.

Question 86: Pharmacology/Chemistry - Sleep Disorders

Discussion:

Sodium oxybate, the sodium salt of gamma-hydroxybutyrate (GHB), an endogenous substance in the brain, is an effective medication in the treatment of daytime sleepiness in narcolepsy. GHB inhibits the release of several neurotransmitters, including GABA, glutamate, and dopamine. Supraphysiologic concentrations appear necessary in order for GHB to bind to GABAB receptors, which is responsible for sleep induction and an increase in slow-wave sleep. The nocturnal sleep effects have been correlated with the improvement in daytime sleepiness in patients with narcolepsy. Sodium oxybate was first described 50 years ago when used as a general anesthetic agent. Consequently, it was administered therapeutically at bedtime to patients suffering from disorders of nocturnal sleep, including narcolepsy, where it was found to reduce nocturnal awakenings, increase stages 3 and 4 (N3) (delta or slow-wave) sleep, and consolidate REM sleep periods. In addition, the improvements in nocturnal sleep were associated with improvements in the daytime symptoms, including cataplexy.

References:

Thorpy MJ. Narcolepsy. Continuum: lifelong learning in neurol 2007;13(3):101-114.

Question 99: Pharmacology/Chemistry - Epilepsy

Discussion:

Benzodiazepines and barbiturates facilitate hyperpolarization by positively modulating a subunit of the GABA-A receptors.

References:

Gibbs JW, McNamara JO. The epilepsies: phenotype and mechanisms. In: Siegel GJ, editor. Basic neurochemistry: molecular, cellular and medical aspects. 7th ed. Amsterdam: Academic press, 2006.

Question 101: Pharmacology/Chemistry - Movement Disorders

Discussion:

Based on American Academy of Neurology criteria, the highest quality literature available for the respective indications is as follows: blepharospasm (two Class II studies); hemifacial spasm (one Class II and one Class III study); cervical dystonia (seven Class I studies); focal upper extremity dystonia (one Class I and three Class II studies); focal lower extremity dystonia (one Class II study); laryngeal dystonia (one Class I study); motor tics (one Class II study); and upper extremity essential tremor (two Class II studies).

Therefore, botulinum neurotoxin should be offered as a treatment option for the treatment of cervical dystonia (Level A), may be offered for blepharospasm, focal upper extremity dystonia, adductor laryngeal dystonia, and upper extremity essential tremor (Level B), and may be considered for hemifacial spasm, focal lower limb dystonia, and motor tics (Level C). Spastic dysphonia is due to upper motor neuron lesions. Though case series have been reported using botulinum toxin for other movement disorders (such as myoclonus and tics), there is not enough evidence, or clinical consensus, to recommend it as first-line therapy.

References:

Simpson DM, Blitzer A, Brashear A, et al. Botulinum neurotoxin for the treatment of movement disorders (an evidence-based review): report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. Neurology 2008;70(19):1699-1706.

Question 119: Pharmacology/Chemistry - Epilepsy

Discussion:

Drugs that inhibit carbamazepine metabolism result in elevated levels and toxicity. These include phenytoin, cimetidine, diltiazem, erythromycin, verapamil, fluoxetine, and isoniazid. Alternately, carbamazepine can accelerate hepatic breakdown of a number of drugs, including its own metabolism. The most common interaction is with oral contraceptives, sodium valproate, ethosuximide, corticosteroids, anticoagulants, antipsychotics, cyclosporine, and methylphenidate. Meperidine and

methylphenidate can lower the seizure threshold in epilepsy patients resulting in worsening seizures independent of antiepileptic therapy.

References:

Ruffmann C, Bogliun G, Beghi E. Epileptogenic drugs: a systematic review. Expert Rev Neurother 2006;6(4):575-589.

Pauwels O. Factors contributing to carbamazepine-macrolide interactions. Pharmacol Res 2002;45(4):291-298.

Question 121: Pharmacology/Chemistry - Neuromuscular Disorders

Discussion:

Myotonia congenita is an inherited neuromuscular disorder characterized by the inability of muscles to quickly relax after a voluntary contraction. The condition is present since early childhood, but symptoms can be mild. Most children will be 2 or 3 years old when parents first notice their muscle stiffness, particularly in the legs and often provoked by sudden activity after rest. The disease does not cause muscle wasting; in fact, it may cause muscle enlargement. Muscle strength is increased. There is an autosomal dominant form (Thomsen) and an autosomal recessive form (Becker), which are both associated with mutations of the gene that codes for the muscle chloride channel CLCN1 on chromosome 7q35. CLCN1 is necessary in order to stabilize the high resting membrane potential of skeletal muscle. Dysfunction of this channel as a result of genetic mutation, causes partial depolarization of the membrane and allows a hyperexcitable state to exist, resulting in myotonia. It is postulated that permanent excitability gives rise to constant mild muscle activity, resulting in muscle hypertrophy. Muscle stiffness responds well to drugs that reduce the associated hyperexcitability of the sarcolemma by interfering with sodium channels located on it. These drugs theoretically reduce spontaneous discharges of electrical myotonia by decreasing the number of available sodium channels, but they have no known effects on chloride channels. One such drug is mexiletine, which is able to reduce myotonia with doses of 200 mg 2 or 3 times a day. Phenytoin 200 mg/d to 300 mg/d can also be used to treat myotonia. A number of overlapping inherited nondystrophic myotonia syndromes result from mutations to the gene encoding the voltage-gated sodium channel type IV alpha subunit (SCN4A). Paradoxical myotonia, in which there is an increase in myotonia with physical activity, and aggravation of myotonia with cold are both indicative of paramyotonia congenita. Transient paralysis indicates hyperkalemic periodic paralysis, and fluctuating myotonia indicates potassium-aggravating myotonia.

References:

Chrestian N, Puymirat J, Bouchard JP, Dupre N. Myotonia congenita – a cause of muscle weakness and stiffness. Nat Clin Pract Neurol 2006;2(7):393-399.

Question 133: Pharmacology/Chemistry - Toxic/Metabolic Disease

Discussion:

Windshield wiper fluid is made of methanol. Both ethylene glycol and methanol are metabolized primarily by the hepatic enzyme alcohol dehydrogenase. Ethanol is also a substrate for alcohol dehydrogenases; It competitively inhibits the metabolism of ethylene glycol or methanol. When ethanol is administered, followed by hemodialysis, both the parent compound and its metabolites are removed. However, ethanol has erratic pharmacokinetics and can cause changes in mental status, hypoglycemia, and pancreatitis. Fomepizole (4-methylpyrazole) is a competitive inhibitor of alcohol dehydrogenase that prevents the formation of metabolites of ethylene glycol and methanol. It is most effective when given early, before significant quantities of metabolites are formed. Given the efficacy of inhibition of alcohol dehydrogenase by fomepizole, the prognosis is primarily dependent on the time from ingestion to the initiation of therapy and the amount of the toxic metabolite that has accumulated, rather than the plasma concentration of the parent compound at the time that fomepizole is administered. Fomepizole was approved in the United States for the treatment of ethylene glycol poisoning in 1997; in 2000, an indication for methanol toxicity was added.

References:

Brent J. Fomepizole for ethylene glycol and methanol poisoning. N Engl J Med 2009;360:2216-2223.

Question 135: Pharmacology/Chemistry - Demyelinating Disorders

Discussion:

Alemtuzumab is a humanized monoclonal antibody against CD52 that causes a long-lasting depletion of lymphocytes and monocytes. Immune-mediated hypothyroidism or hyperthyroidism occurs in more than 30% of patients treated with alemtuzumab. Idiopathic thrombocytopenia has been detected in 1?3% of patients, and a few patients have developed renal failure secondary to Goodpasture syndrome.

References:

Sorensen PS. New management algorithms in multiple sclerosis. Current Opinion in Neurology. 27(3):246-59, 2014 Jun.

Question 136: Pharmacology/Chemistry - Neuromuscular Disorders

Discussion:

Nusinersen has been shown to improve motor function in patients with spinal muscular atrophy (SMA). SMA is most commonly associated with mutations in the survival motor neuron 1 (SMN1) gene. Humans possess a second SMN gene, SMN2. SMN2 and SMN1 are related by an inverted gene duplication. SMN2 contains a C-to-T mutation in exon 7 that redirects alternative splicing to exclude exon 7 and leads to an unstable mature protein that cannot substitute for mutant SMN1. Nusinersen is an antisense oligonucleotide that inhibits the splicing of exon 7 on the SMN2 gene resulting in increased levels of stable SMN protein.

References:

David R Corey. Nusinersen, an antisense oligonucleotide drug for spinal muscular atrophy. Nature Neuroscience 20, 497?499 (2017)

Question 145: Pharmacology/Chemistry - Headache

Discussion:

Erenumab is a monoclonal antibody that binds specifically to the calcitonin gene-related protein receptor. It does not bind to the amylin receptor although both receptors are similar. Galcanezumab, eptinezumab, and fremanezumab are other newly-developing monoclonal antibodies that bind to the calcitonin gene-related protein ligand.

References:

Maasumi K, Michael RL, Rapoport AM. CGRP and Migraine: The Role of Blocking Calcitonin Gene-Related Peptide Ligand and Receptor in the Management of Migraine.. Drugs. 2018 Jun;78(9):913-928. doi: 10.1007/s40265-018-0923-5.

Question 150: Pharmacology/Chemistry - Movement Disorders

Discussion:

The radiolabeled tracer I-123 Ioflupane used in I-FP-CIT (DaT) SPECT scans binds to the presynaptic dopamine re-uptake channels in the projection neurons that start in the substantia nigra and terminate in the striatum. Bupropion inhibits norepinephrine and dopamine reuptake through this channel and thus can inhibit uptake of the radiolabeled tracer I-123 Ioflupane. This causes the DaT scan to appear falsely positive. Risperidone is a dopamine receptor blocker with effects on the post-synaptic side and does not affect DaT scan. Carbidopa/levodopa is metabolized to dopamine and does not effect the specificity of the DaT scan nor does pramipexole or amantadine.

References:

Darcourt J1, Booij J, Tatsch K, Varrone A, Vander Borght T, Kapucu OL, N妆en K, Nobili F, Walker Z, Van Laere K.. EANM procedure guidelines for brain neurotransmission SPECT using (123)I-labelled dopamine transporter ligands, version 2.. European Journal of Nuclear Medicine and Molecular Imaging, February 2010, Volume 37, Issue 2, pp 443?450 |

Question 153: Pharmacology/Chemistry - Demyelinating Disorders

Discussion:

This patient presents with a form fruste of area postrema syndrome as an early manifestation of NMO spectrum disorder (NNOSD) and aquaporin-4 autoimmunity. Approximately 10% of patients with NMOSD present with intractable nausea, vomiting, and hiccups. Aquaporin-4 water channel is highly expressed on astrocytic foot processes in circumventricular regions of the brainstem (area postrema, subfornical organ (SFO), organum vasculosum lamina terminalis (OVLT), all regions that lack a blood-brain barrier (BBB). The absence of BBB in these areas may result in preferential entry of aquaporin-4 antibody in patients with NMOSD, producing a unique variety of symptoms referable to these regions. Involvement of the area postrema produces intractable nausea, vomiting, and hiccoughs, whereas SFO/OVLT lesions manifest with hypothalamic dysfunction (e.g. hypersomnolence, narcolepsy, and SIADH).

References:

Pittock SI, Lucchinetti CF. Neuromyelitis optica and the evolving spectrum of autoimmune aquaporin-4 channelopathies: a decade later. Ann N Y Acad Sci. 2015 Jun 10.

Question 159: Pharmacology/Chemistry - Headache

Discussion:

In April of 2018, the FDA approved a small, hand held, non-invasive vagus nerve stimulator that applies an electric current to the skin and underlying supraorbital nerves based on 2 double-blinded, randomized, sham-controlled trials, ACT 1 and ACT 2. In ACT 1, Response rates defined as the proportion of subjects who achieved pain relief (pain intensity of 0 or 1) at 15 minutes after treatment initiation for the first CH attack without rescue medication use through 60 minutes were significantly higher with nVNS than with sham for the eCH cohort (nVNS, 34.2%; sham, 10.6%; P=.008). In ACT2, a significantly higher percentage of attacks were pain-free (defined as pain-free at 15 minutes after the onset of pain from cluster headache with no use of rescue medication through the 30-minute treatment period) in patients treated with vagus nerve stimulator (47.5%) versus placebo (6.2%; p=0.003). There are numerous case reports of the efficacy of deep brain stimulation of the posterior hypothalamus in the treatment of cluster headache. Similarly, percutaneous stimulation to the sphenopalatine ganglion appeared effective in a small randomized control trial of the treatment of intractable cluster headache but this has not been FDA-approved.

References:

FDA Releases gammaCore, the First Non-Invasive Vagus Nerve Stimulation Therapy Applied at the Neck for Acute Treatment of Pain Associated with Episodic Cluster Headache in Adult Patients. https://www.electrocore.com/news/fda-releases-gammacore-the-first-non-invasive-vagus-nerve-stimulation-therapy-applied-at-the-neck-for-acute-treatment-of-pain-associated-with-episodic-cluster-headache

Silberstein SD; Mechtler LL; Kudrow DB; Calhoun AH; McClure C; Saper JR; Liebler EJ; Rubenstein Engel E; Tepper SJ; ACT1 Study Group.. Non-Invasive Vagus Nerve Stimulation for the ACute Treatment of Cluster Headache: Findings From the Randomized, Double-Blind, Sham-Controlled ACT1 Study.. Headache. 56(8):1317-32, 2016 Sep.

Question 171: Pharmacology/Chemistry - Neuromuscular Disorders

Discussion:

This patient's EMG is consistent with a pure sensory disorder since there is loss of sensory nerve conduction responses with sparing of motor nerve conduction responses and normal motor unit action potentials on needle EMG examination. The global loss of sensory nerve conduction responses suggests a neuronopathy instead of a length dependent axonal sensory neuropathy. Causes of a sensory neuronopathy include Sjogren syndrome, paraneoplastic syndrome usually with an anti-HU antibody, pyridoxine intoxication (al least 200 mg per day), a variant of Guillain-Bare syndrome, and with platinum-based chemotherapies.

References:

Kuntzer T. Antoine JC. Steck AJ.. Clinical features and pathophysiological basis of sensory neuronopathies (ganglionopathies).. Muscle & Nerve. 2004; 30(3):255-68

Question 172: Pharmacology/Chemistry - Epilepsy

Discussion:

Bupropion can reduce the seizure threshold in 1 out of 1000 patients. However, in patients with bulimia and anorexia nervosa, the seizure risk may be particularly higher.

References:

Hughes JR, Stead LF, Lancaster T. Antidepressants for smoking cessation. Cochrane Database Syst Rev 2007 Jan 24;(1):CD000031.

Question 173: Pharmacology/Chemistry - Sleep Disorders

Discussion:

This patient has three cardinal symptoms of narcolepsy (excessive daytime sleepiness, hypnagogic hallucinations, and cataplexy. Primary narcolepsy is a putative autoimmune disorder in which there is loss of hypocretinergic neurons in the lateral and preforniceal hypothalamus. Hypocretin deficiency results in loss of centrally mediated motor activation that occurs in response to emotional stimuli, producing cataplexy. Patients with narcolepsy have reduced levels of hypocretin in CSF (< 110 pg/ml).

References:

Thorpy MJ. Narcolepsy. Continuum 2007;13(3):101-114.

Question 174: Pharmacology/Chemistry - Movement Disorders

Discussion:

Wilson's disease is an autosomal recessive disease associated with mutations of the copper-transporting ATPase gene on chromosome 13q14.3. Clinical features are neurological (40%), hepatic (40%), and psychiatric (15%). Patients present in the second or third decade of life. Neurologic features include an akinetic-rigid syndrome resembling parkinsonism, generalized dystonia, or postural tremor with ataxia. Dysarthria and clumsiness of the hands are common presenting features. Kayser-Fleischer rings are present in virtually all patients with neurological features. The pathologic abnormalities are primarily in the basal ganglia, with cavitary necrosis of the putamen and caudate, in addition to cortical atrophy. The liver develops a nodular cirrhosis.

In most cases Wilson's disease can be diagnosed by measurement of the serum concentration of the copper protein, ceruloplasmin, which is often low (<20mg/dl). Serum total copper is low in many patients and urinary copper excretion is always raised. Definitive investigation is a liver biopsy with measurement of copper concentration.

D-penicillamine with pyridoxine is the gold standard of treatment. Alternative therapies include trientene, zinc, tetrathiomolybdate, dimercapol, and liver transplantation. Symptomatic treatment with antiparkinsonism drugs may be of benefit.

References:

Lorincz MT.. Neurologic Wilson's disease.. Ann N Y Acad Sci. 2010 Jan;1184:173-87.

Question 177: Pharmacology/Chemistry - Neurogenetics

Discussion:

Subependymal giant cell astrocytoma (SEGA) is a brain tumor associated with tuberous sclerosis (TSC). Aberrant hyperactivity of mammalian target of rapamycin (mTOR) is caused by a mutation in one of the two TSC genes, TSC1 and TSC2, which results in cellular proliferation and tumor growth. The use of mTOR inhibitors, particularly everolimus, has been shown to reduce both SEGA size and seizure frequency. Surveillance for SEGA by imaging study is therefore recommended. mTOR inhibitors also may be useful in treating renal angiomyolipomas in patients with TSC.

References:

Krueger DA, Care MM, Holland K, et al.. Everolimus for subependymal giant-cell astrocytomas in tuberous sclerosis. N Engl J Med 2010;363:1801-11

Capal JK, Franz DN.. Profile of everolimus in the treatment of tuberous sclerosis complex: an evidence-based review of its place in therapy. Neuropsychiatr Dis Treat 2016;12:2165-72.

Question 195: Pharmacology/Chemistry - Cerebrovascular Disease

Discussion:

Dabigatran, an FDA-approved oral anticoagulant, is a direct thrombin inhibitor (DIT) that was demonstrated to reduce the incidence of stroke and systemic emboli compared with dose-adjusted warfarin in patients with non-valvular atrial fibrillation (AF), while concomitantly decreases the risk of bleeding in a pivotal study (Randomized Evaluation of Long-term Anticoagulant Therapy, or RE-LY). Two other new oral anticoagulants, apixaban and rivaroxaban, inhibit factor Xa, and have also demonstrated non-inferiority with warfarin in patients with AF in prevention of stroke, with a lower bleeding risk.

References:

Alberts, MJ. Antithrombotic therapy for secondary stroke prevention. Continuum Lifelong Learning Neurol 2011; 17(6):1255-1266.

Connolly SJ, Ezekowitz MD, Yusuf S, et al. RE-LY Steering Committee and Investigators.. Dabigatran versus warfarin in patients with atrial fibrillation.. N Engl J Med 2009;361:1139-1151.

Question 303: Pharmacology/Chemistry - Neuromuscular Disorders

Discussion:

Statins are frequently used in cerebrovascular and cardiovascular diseases in an attempt to reduce the vascular risk. Myositis is one of the well-known side-effects from statin therapy and is often resolved after discontinuation. Autoimmune necrotizing myopathy has been discovered in patients using statins. The autoantibody is directed against HMG CoA reductase enzyme. Clinically, the weakness will continue to progress with serum creatine kinase exceeding 10 times the upper limit. Electromyographic changes are consistent with active myopathic process and MRI frequently reveals muscle edema. Statin-associated autoimmune necrotizing myopathy typically requires immunosuppressive therapy.

References:

Mammen AL. Statin-associated autoimmune myopathy. N Engl J Med 2016;374:664-9

Question 319: Pharmacology/Chemistry - Cerebrovascular Disease

Discussion:

Andexanet alfa is a specific reversal agent that is designed to neutralize the anticoagulant effects of both direct and indirect factor Xa inhibitors. Andexanet is a recombinant modified human factor Xa decoy protein that is catalytically inactive but that retains the ability to bind factor Xa inhibitors in the active site with high affinity. Andexanet binds and sequesters factor Xa inhibitors within the vascular space, thereby restoring the activity of endogenous factor Xa and reducing levels of anticoagulant activity, as assessed by measurement of thrombin generation and anti-factor Xa activity. Among the apixaban-treated participants, anti-factor Xa activity was reduced by 94% among those who received an andexanet bolus (24 participants), as compared with 21% among those who received placebo (9 participants) ($P<0.001$), and thrombin generation was fully restored in 100% versus 11% of the participants ($P<0.001$) within 2 to 5 minutes. Among the rivaroxaban-treated participants, anti-factor Xa activity was reduced by 92% among those who received an andexanet bolus (27 participants), as compared with 18% among those who received placebo (14 participants) ($P<0.001$), and thrombin generation was fully restored in 96% versus 7% of the participants ($P<0.001$). Andexanet alfa was approved by the FDA in May of 2018. Idarucizumab is a humanized monoclonal antibody fragment that has been developed as a specific reversal agent for dabigatran.

References:

Deborah M. Siegal, M.D., John T. Curnutte, M.D., Ph.D., Stuart J. Connolly, M.D., Genmin Lu, Ph.D., Pamela B. Conley, Ph.D., Brian L. Wiens, Ph.D., Vandana S. Mathur, M.D., Janice Castillo, B.S., Mich. Andexanet Alfa for the Reversal of Factor Xa Inhibitor Activity. N Engl J Med 2015; 373:2413-2424

Question 320: Pharmacology/Chemistry - Toxic/Metabolic Disease

Discussion:

Excessive zinc ingestion is a well-recognized cause of copper deficiency. In addition to the common use of zinc in the prevention or treatment of common colds and sinusitis, zinc therapy has been used for conditions such as acrodermatitis enteropathica, decubitus ulcers, sickle cell disease, celiac disease, memory impairment, and acne. Unusual sources of excess zinc have included a patient who consumed an entire tube of a denture cream that contained zinc daily for 5 years and patients swallowing coins containing zinc. Zinc causes an upregulation of metallothionein production in the enterocytes. Metallothionein is an intracellular ligand, and copper has a higher affinity for metallothionein than zinc. Copper displaces zinc from metallothionein, binds preferentially to the metallothionein, remains in the enterocytes, and is lost in the feces as the intestinal cells are sloughed.

Subsequent copper deficiency is recognized caused of subacute combined degeneration, similar to that associated with B12 deficiency.

References:

Kumar N.. Copper deficiency myelopathy (human swayback).. Mayo Clin Proc. 2006 Oct;81(10):1371-84.

Hedera P. Peltier A. Fink JK. Wilcock S. London Z. Brewer GJ.. Myelopolyneuropathy and pancytopenia due to copper deficiency and high zinc levels of unknown origin II. The denture cream is a primary source of excessive zinc. Neurotoxicology; 2009; 30(6):996-9,

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Question 325: Pharmacology/Chemistry - Toxic/Metabolic Disease

Discussion:

Food poisoning producing gastrointestinal and sensorimotor symptoms beginning within 24 hours of ingestion of tropical reef fish or their predators is termed ciguatera. Ciguatera is the most common reportable food poisoning associated with seafood. Most cases, however, go unreported to state health authorities. The annual incidence in the United States has been estimated to be as high as approximately 1:2000 and in the South Pacific as high as approximately 1:1000.

The toxin is produced by marine microorganisms and then passed up the food chain from herbivorous reef fish to carnivorous reef predators to man. Clinical syndromes may vary, depending on the predominant toxin. Ciguateric toxins are thermostable and unaffected by cooking, freezing, or salting. Affected fish look, smell, and taste normal. Toxin concentrations are generally greatest in larger and older reef predators, such as barracuda, and are concentrated in the visceral organs, roe, and brains of affected fish.

References:

Watters MR. Neurologic marine biotoxins. Continuum: lifelong learning in neurol 2008;14(5):81-101.

Question 327: Pharmacology/Chemistry - Movement Disorders

Discussion:

The use of anticholinergic agents such as trihexyphenidyl in Parkinson disease (PD) is typically reserved for younger patients (under 60 years old) with tremor-predominant dysfunction. Other cardinal features of PD, such as bradykinesia, postural instability, and rigidity, are generally unresponsive to anticholinergic medication. Anticholinergic agents should not be prescribed to older patients and patients with dementia due to their wide adverse side effect profile, including cognitive dysfunction, urinary retention, dry mouth, and gastrointestinal disturbances.

References:

Olanow CW, Stern MB, Sethi K. The scientific and clinical basis for the treatment of Parkinson disease. Neurology 2009;72 (Suppl 4):S1-S136.

Question 329: Pharmacology/Chemistry - Neuromuscular Disorders

Discussion:

Autoimmune autonomic ganglionopathy (AAG) is characterized by prominent and selective involvement of the peripheral autonomic nervous system. Patients typically develop generalized autonomic failure including orthostatic hypotension, anhidrosis, and parasympathetic dysfunction. Sensory nerve involvement may also occur, producing acral paresthesias and dysesthesias; motor nerves are generally spared. The onset can be acute, subacute, or gradual. The course is variable, with spontaneous improvement occurring in about one-third of patients,1 but recovery is typically incomplete. This disorder can be associated with serum antibodies to ganglionic acetylcholine receptor. Treatment with IVIg or plasma exchange may hasten recovery, as in acute inflammatory demyelinating polyneuropathy (AIDP). Unlike AIDP, prednisone may be useful in this disorder.

References:

Iodice V, Kimpinski K, Vernino S, Sandroni P, Fealey RD, Low PA.. Efficacy of immunotherapy in seropositive and seronegative putative autoimmune autonomic ganglionopathy. Neurology. 2009 Jun 9;72:2002-8.

Question 338: Pharmacology/Chemistry - Demyelinating Disorders

Discussion:

Paraneoplastic cerebellar degenerations are disorders of the cerebellum, the part of the brain responsible for coordination, and are associated with tumors (neoplasms). They arise when tumors express proteins that are normally found only in neurons, and it is believed that the immune system, in its attempt to kill the tumor, also damages the cerebellum. Certain tumors are more common than others. These include cancer of the ovary, uterus, or adnexa, cancer of the breast, and especially small cell carcinoma of the lung. The condition frequently begins before the tumor is diagnosed.

Pathological examination often reveals profound loss of Purkinje cells, which are the output cells for the cerebellum. The MRI scan of the brain may be normal. Anti-Yo is the anti-Purkinje cell antibody and reacts only with Purkinje cells. Patients with anti-Yo have a gynecological cancer, ovarian or breast 90% of the time. Anti-Hu reacts with nearly all neurons and is commonly associated with sensory neuropathy and encephalomyeloneuropathy.

References:

Bataller L, Dalmau J. Paraneoplastic neurologic syndromes: approaches to diagnosis and treatment. Semin Neurol 2003;23:215-224.

Question 339: Pharmacology/Chemistry - Cerebrovascular Disease

Discussion:

Contraindications to the use of recombinant tissue type plasminogen activator in acute ischemic stroke include international normalized ratio (INR) of 1.7 or greater, major surgery in the 14 days prior to stroke; platelet count less than 100,000 / mm3; CT demonstrating hypodensity greater than one-third cerebral hemisphere; and onset of symptoms greater than 270 minutes prior to administration. Apixaban is a direct factor XA inhibitor but no rapid assay of factor XA activity is available in the setting of acute ischemic stroke. The half-life of apixaban is 12 hours, requiring at least 48-hour discontinuance for safe administration of rtPA in this setting.

References:

Jauch EC, Saver JC, Adams HP, et al.. Guidelines for the Early Management of Patients With Acute Ischemic Stroke A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association. Stroke. 2013;44:870-947.

Khatri P, Levine J, Jovin T. Intravenous thrombolytic therapy for acute ischemic stroke. Continuum: lifelong learning neurology 2008;14:46-60.

Question 346: Pharmacology/Chemistry - Neuromuscular Disorders

Discussion:

More than 30 medications have been reported to have an effect on neuromuscular transmission. A variety of drugs induce or worsen myasthenic symptoms through actions on pre- or postsynaptic mechanisms. Certain antibiotics impair transmitter release by interfering with calcium flux. Other drugs affect metabolism of acetylcholine or cholinergic receptor function. There are numerous case reports of commonly used medications suspected in exacerbations or first presentations of myasthenia gravis. These include anti-hypertensives such as beta-blockers and calcium channel blockers, antibiotics, such as aminoglycosides, quinolones, telithromycin, azithromycin, erythromycin, clindamycin, ampicillin, imipenem, vancomycin, metronidazole, antiarrhythmics, such as quinidine, lidocaine, procainamide, and other agents, such as lithium, phenytoin, prednisone, and hydroxychloroquine.

References:

Sanders DB, Howard JF Jr. Disorders of neuromuscular transmission. In: Bradley WG, Daroff RB, Fenichel GM, et al, editors. Neurology in clinical practice. 3rd ed. Boston: Butterworth-Heinemann, 2000.

Question 362: Pharmacology/Chemistry - Demyelinating Disorders

Discussion:

Dalfampridine is a potassium-channel blocker that improves nerve conduction along centrally demyelinated axons and has been demonstrated to improve ambulation speed in approximately one-third of patients with multiple sclerosis. The drug carries a 0.2% risk of seizures, which is usually associated with toxic blood levels. Fampridine is cleared unchanged by the kidneys and is contraindicated in patients with creatinine clearance (GFR) of less than 50 cc/min because of the resultant risk of developing seizures. The risk of seizures in patients with GFR of 51-80 is uncertain.

References:

AD Goodman, TR Brown, JA Cohen, et al. Dose comparison trial of sustained-release fampridine in multiple sclerosis. Neurology 2008;71:1134-1141.

Question 371: Pharmacology/Chemistry - Sleep Disorders

Discussion:

Lewy body dementia, Parkinson disease, and multiple system atrophy are all associated with REM behavior disorder, which may present up to decades prior to the onset of the neurodegenerative illness. These disorders are all characterized by abnormal deposition of alpha-synuclein in the cytoplasm of neurons and glial cells and are grouped histopathologically as synucleinopathies. The treatment of choice for REM behavior disorder is clonazepam; melatonin and pramipexole have also demonstrated benefit in small case series.

References:

RR Auger, BF Boeve. Sleep and neurodegenerative disorders. Continuum Lifelong Learning Neurol 2007;13:201-224.

Question 400: Pharmacology/Chemistry - Epilepsy

Discussion:

Topamax has been known to cause a potentially serious condition known as metabolic acidosis (an increase of acid in the blood). In children, chronic metabolic acidosis may affect growth or cause rickets (a softening or weakness of the bones that can lead to bone deformities). A doctor should be contacted immediately if one experiences symptoms of metabolic acidosis such as rapid breathing, an irregular heartbeat, confusion, lethargy, fatigue, or loss of appetite.

References:

Available from. :www.topamax.com/topamax/tools-resources--safety-information.html. accessed March 1, 2010.

Physiology

Question 1: Physiology - EMG

Discussion:

Nerve conduction studies assess the facial nerve distal to the stylomastoid foramen. Abnormalities of the needle EMG do not localize the lesion to the nerve other than distal to the nucleus. The blink reflex assesses the full length of the nerve and gives useful information about the segment proximal to the stylomastoid foramen.

References:

Preston & Shapiro. Electromyography and Neuromuscular Disorders: Clinical-Electrophysiologic Correlations. 3rd edition, Elsevier Saunders, 2013

Question 11: Physiology - Sleep

Discussion:

Kleine-Levin syndrome is a sleep disorder predominant in adolescent males with bouts of excessive sleeping up to 18 hours per day in episodes lasting 7-14 days and associated with hypersexual behavior, either anorexia or hyperphagia, feeling of depersonalization and cognitive issues. Hypocretin and orexin levels are reduced during episodes. Treatment is with either lamotrigine or lithium.

References:

Kotagal S. Sleep Wake Disorders of Childhood. Continuum 2017; 23: 1132-1150

Question 20: Physiology - Basic Physiology

Discussion:

Cold temperatures cause slowing of conduction of the action potential. This results in slowing of conduction velocity, prolongation of distal motor latency, and increase in size of CMAP and SNAP, due to reduction in phase cancellation amongst the axons in the nerve.

References:

Preston DC, Shapiro BE. Electromyography and neuromuscular disorders: clinical-electrophysiologic correlations. 3nd ed. Philadelphia: Elsevier, 2012.

Question 23: Physiology - Sleep

Discussion:

This patient has REM sleep behavior disorder (RBD). RBD is characterized by abnormal motor activity, often associated with frightening and violent dreams and occur during REM sleep. More than 30-40% of patients with chronic RBD develop Parkinson disease, multisystem atrophy or Lewy body dementia--all synuclein disorders. Polysomnography demonstrates increased chin EMG activity or increased upper or lower extremity surface EMG findings during REM sleep.

References:

Kryger MH, Roth T, Dement WC. Principles and practice of sleep medicine. 5th ed. Philadelphia: Saunders, 2010.

Hogl B and Iranzo A. Rapid Eye Movement Sleep Behavior Disorder and other rapid eye movement sleep parasomnias. Continuum 2017; 23: 1017-34

Question 24: Physiology - Autonomic Studies

Discussion:

Patients with small fiber axonal neuropathy secondary to diabetes may have normal nerve conduction studies/EMG but autonomic testing may be abnormal.

References:

Preston & Shapiro. Electromyography and Neuromuscular Disorders: Clinical-Electrophysiologic Correlations. 3rd edition, Elsevier Saunders, 2013

Question 34: Physiology - Autonomic Studies

Discussion:

Acetylcholine is the primary postganglionic neurotransmitter at all parasympathetic neuroeffector junctions. Norepinephrine is the primary postganglionic neurotransmitter at most sympathetic neuroeffector junctions.

References:

Steven Vernino; Roy Freeman. PERIPHERAL AUTONOMIC NEUROPATHIES. Continuum: Autonomic Disorders p. 89-110 December 2007, Vol.13, No.6

Question 47: Physiology - EEG

Discussion:

For absence seizures, hyperventilation is still the best activation procedure for bringing out abnormalities on the EEG.

References:

Ebersole, J.S., Husain A.M., Nordli, D.R.. Current Practice of Clinical Electroencephalography. 4th Edition. Philadelphia: Wolters Kluwer, 2014

Question 60: Physiology - EMG

Discussion:

This patient presents with the clinical picture of a radiculopathy with his pattern of deficits pointing towards C4-7 (DTRs 5 and 6, shoulder abduction 5, elbow flexion 5,6, wrist flexion 6-T1, sensory change 4-6). The needle exam reveals fibrillation potentials in the biceps (a 5,6 muscle) and pronator teres (a 6,7 muscle). The "common root" would be C6.

References:

Preston DC, Shapiro BE. Electromyography and neuromuscular disorders: clinical-electrophysiologic correlations. 3nd ed. Philadelphia: Elsevier, 2012.

Question 70: Physiology - Basic Physiology

Discussion:

Patients with myotonia congenita have normal muscle strength and bulk with myotonia as the prominent symptom and sign. This is a chloride channelopathy.

References:

Valeria A. Sansone, MD. The Dystrophic and Nondystrophic Myotonias. The Dystrophic and Nondystrophic Myotonias in Continuum: Muscle and Neuromuscular Junction Disorders p. 1889-1915 December 2016, Vol.22, No.6

Question 72: Physiology - EMG

Discussion:

The clinical description is classic for carpal tunnel syndrome. Of the choices, median sensory studies are the most sensitive in mild carpal tunnel syndrome. Motor distal latency prolongation and EMG abnormalities in the median territory occur later in the condition and indicate more severe nerve compression. The other options pertain to nerves unaffected by carpal tunnel syndrome: ulnar and radial, respectively.

References:

Preston & Shapiro. Electromyography and Neuromuscular Disorders: Clinical-Electrophysiologic Correlations. 3rd edition, Elsevier Saunders, 2013

Question 75: Physiology - EMG

Discussion:

Sensory studies aid in the localization of pre- or post- dorsal root ganglion lesions. Lesions proximal to dorsal root ganglia, like radiculopathy, have normal sensory nerve action potentials. Sensory nerve action potentials are abnormal in lesions distal to dorsal root ganglia. The abductor pollicis brevis muscle is innervated by the median nerve with radicular derivation from C8 and T1. The first dorsal interosseous muscles are innervated by the ulnar nerve and is supplied by radicular contributions from C8 and T1. The extensor indicis proprius muscles are innervated by the radial nerve and is supplied by radicular contributions from C8. All of the above three muscles are innervated by the lower trunk of the brachial plexus and any abnormality there might produce low amplitudes in the median and ulnar motor nerve action potentials.

References:

Preston & Shapiro. Electromyography and Neuromuscular Disorders: Clinical-Electrophysiologic Correlations. 3rd edition, Elsevier Saunders, 2013

Question 83: Physiology - Sleep

Discussion:

The apnea hypopnea index (AHI) is the number of apneas and hypopneas per hour of sleep - calculated as the total number recorded divided by total sleep time. The respiratory disturbance index (RDI) is the number of apneas, hypopneas, and respiratory effort related arousals per hour of sleep.

References:

Lee-Chiong, Teofilo. Sleep Medicine: Essentials and Review. Oxford: Oxford University Press, 2008.

Question 90: Physiology - EMG

Discussion:

The proximity of the sciatic nerve explains its vulnerability during hip replacement surgery. The peroneal division of this nerve is often more severely affected. The abnormalities of the superficial peroneal and sural sensory nerve action potentials serve to localize the lesion distal to the dorsal root ganglion and argue against a lumbosacral root lesion. The innervation of the short head of the biceps femoris and anterior tibialis muscles both come from the peroneal division of the sciatic nerve.

References:

Distad, BJ and Weiss MD. Clinical and Electrodiagnostic Features of Sciatic Neuropathies. Phys Med Rehabil Clin N Am, 2013; 24:107-120

Ropper AH, Zafonte RD. Sciatica. N Engl J Med. 2015;372:1240-8.

Question 95: Physiology - Evoked Potentials

Discussion:

Somatosensory evoked potentials record activity in the dorsal column/medial lemniscal sensory pathways. Neurons in the spinothalamic tracts and spinoreticulothalamic systems have small diameter axons and are not recordable with standard SEP techniques. Propriospinal neurons interconnect adjacent regions of the spinal cord and do not contribute to the SEP. The ventral spinocerebellar tract ascends to the midbrain then enters through the superior cerebellar peduncle. It does not contribute to the SEP signal.

References:

Daube JR, editor. Clinical neurophysiology. New York: Oxford University Press, 2009.

Question 97: Physiology - EEG

Discussion:

Attenuation or blocking of the alpha rhythm or posterior dominant rhythm due to heightened mental activity such as performing complex mental arithmetic may not be present in most cases, but it can be a well described normal response on EEG. An occipital lesion may cause an asymmetric response to eye opening (Bancaud phenomenon). Drowsiness, encephalopathy and inattention can impede the blocking of the alpha rhythm.

References:

Schomer D and Lopez de Silva F. Niedermeyer's Electroencephalography: Basic Principles, Clinical Applications, and Related Fields. Philadelphia, PA, Lippincott Williams & Wilkins, 2018

Question 113: Physiology - EMG

Discussion:

In a lesion of the peroneal division of the sciatic nerve, the short head of the biceps femoris muscle will show evidence of denervation in addition to the tibialis anterior and peroneus longus muscles. Sparing of AH indicates this is not a tibial neuropathy; sparing of AH and semitendinosus argues against involvement of the tibial division of the sciatic nerve/sciatic neuropathy. Sparing of gluteus medius argues against L5 radiculopathy.

References:

Preston DC, Shapiro BE. Electromyography and neuromuscular disorders: clinical-electrophysiologic correlations. 3nd ed. Philadelphia: Elsevier, 2012.

Question 120: Physiology - Sleep

Discussion:

Sleep spindles are required to be present on an EEG to make a determination of Stage 2 non-REM sleep. Vertex waves or sharp transients of sleep are seen in both Stage 1 and Stage 2, while saw-tooth waves are seen in REM sleep. Generalized delta is seen in Stage 3 while positive occipital sharp transients of sleep are a benign variant of non-REM sleep.

References:

Silber MH. Diagnostic approach and investigation in sleep medicine. Continuum 2017; 23: 973-988

Question 123: Physiology - EMG

Discussion:

Sensory responses are affected in lesions distal to the dorsal root ganglion (i.e. plexopathies) while they are spared in lesions proximal to the dorsal root ganglion (i.e. radiculopathies). Thus, they are quite useful in distinguishing between root and plexus lesions.

References:

Preston DC, Shapiro BE. Electromyography and neuromuscular disorders: clinical-electrophysiologic correlations. 3nd ed. Philadelphia: Elsevier, 2012.

Question 124: Physiology - EMG

Discussion:

Pompe disease, infantile acid maltase deficiency, is an autosomal recessive glycogen storage disorder that causes generalized hypotonia, cardiomyopathy, hepatomegaly and macroglossia. Needle EMG shows myopathic features and electrical myotonia without evidence of clinical myotonia. Prader Willi syndrome presents with neonatal hypotonia, feeding problems with excessive weight gain, hypogonadism, and narrow faces with almond-shaped eyes. Myotonia congenita is an autosomal dominant disorder associated with muscle hypertrophy and myotonic discharges on needle EMG. Congenital myotonic dystrophy presents with severe hypotonia, facial diplegia, and dysphagia, but myotonia is not seen at birth. Nemaline myopathy causes proximal weakness with cardiomyopathy, but myotonic discharges are not seen on needle EMG.

References:

Tabon, Alejandro. Metabolic Myopathies.. Continuum: Lifelong Learning in Neurology. Volume 19, Issue 6 Muscle Disease (2013).

Question 127: Physiology - EEG

Discussion:

Spindles are generated within the thalamus in the reticular neurons.

References:

Schomer D and Lopez de Silva F. Niedermeyer's Electroencephalography: Basic Principles, Clinical Applications, and Related Fields. Philadelphia, PA, Lippincott Williams & Wilkins, 2018

Question 139: Physiology - Basic Physiology

Discussion:

Ethosuximide, used to treat absence seizures, binds to calcium channels in the thalamus.

References:

Kandel ER, Schwartz JH, Jessel TM. Principles of neural science. 4th ed. New York: McGraw-Hill, 2000.

Question 168: Physiology - EMG

Discussion:

F waves assess the entire length of the motor axon and can be used as a good internal control for other nerve conduction abnormalities. They may have their greatest usefulness in identifying early polyradiculopathy such as seen in Guillain-Barre syndrome (GBS). Early in GBS, the routine motor nerve conduction studies may be entirely normal, with prolonged or absent F responses, a combination that implies proximal demyelination.

References:

Preston & Shapiro. Electromyography and Neuromuscular Disorders: Clinical-Electrophysiologic Correlations. 3rd edition, Elsevier Saunders, 2013

Question 169: Physiology - Evoked Potentials

Discussion:

During auditory evoked potential recording, wave I represents the distal action potential of cranial nerve VIII. The absence of wave I does not allow an appropriate assessment of central auditory conduction. Occasionally a needle electrode in the external auditory canal may help register this wave if it cannot be recorded with a conventional earlobe electrode.

References:

Daube JR, editor. Clinical neurophysiology. New York: Oxford University Press, 2009.

Question 179: Physiology - EEG

Discussion:

The EEG can provide confirmatory evidence of brain death, which is manifested by an absence of spontaneous or induced electrical activity of cerebral origin. Electrocerebral inactivity (ECI) is defined as "no EEG activity over 2 microvolts." There are important minimal technical criteria for recording in patients with suspected cerebral death, one of which is a minimum of 8 recording scalp electrodes.

References:

Stecker MM1, Sabau D, Sullivan L, Das RR, Selioutski O, Drislane FW, Tsuchida TN, Tatum WO 4th. American Clinical Neurophysiology Society Guideline 6: Minimum Technical Standards for EEG Recording in Suspected Cerebral Death.. Journal of Clinical Neurophysiology. 33(4):324?327, AUG 2016

Daube JR, editor. Clinical neurophysiology. New York: Oxford University Press, 2009.

Question 181: Physiology - EMG

Discussion:

Single fiber EMG (SFEMG) is the most sensitive diagnostic test for myasthenia gravis. In generalized disease, SFEMG examination of a weak muscle demonstrates increased jitter in more than 90% of cases. Slow repetitive stimulation of a distal muscle is approximately 50% sensitive. Repetitive stimulation of a proximal muscle has a higher yield (approximately 75%). Rapid repetitive stimulation (more than 10 hz) is used in presynaptic disorders of neuromuscular transmission.

References:

Amato AA, Russell JA. Neuromuscular disorders. 1st ed. New York: McGraw Hill Medical, 2008.

Question 207: Physiology - EEG

Discussion:

Triphasic waves, though non-diagnostic, are most commonly seen in the context of a metabolic disturbance and particularly with hepatic or renal dysfunction.

References:

Schomer D and Lopez de Silva F. Niedermeyer's Electroencephalography: Basic Principles, Clinical Applications, and Related Fields. Philadelphia, PA, Lippincott Williams & Wilkins, 2018

Question 209: Physiology - EMG

Discussion:

In cases of partial or gradual denervation, reinnervation usually occurs through collateral sprouting by adjacent surviving motor units. As the number of muscle fibers per motor unit increases, MUAPs become prolonged in duration, with a high amplitude, and polyphasic. These MUAP changes, in conjunction with decreased recruitment, are the hallmarks of reinnervated motor units and nearly always imply chronic neuropathic disease (ie, disorders of the anterior horn cell, nerve root, or peripheral nerve). Long duration, high amplitude, polyphasic MUAPs are never seen in acute conditions. When present, they always imply that the process has been present for at least several weeks; more often for months or years.

References:

Preston & Shapiro. Electromyography and Neuromuscular Disorders: Clinical-Electrophysiologic Correlations. 3rd edition, Elsevier Saunders, 2013

Question 215: Physiology - EEG

Discussion:

14- and 6-per-second positive spikes are a benign phenomenon in the EEG and are seen over posterior and temporal head regions during drowsiness and light sleep.

References:

Ebersole, J.S., Husain A.M., Nordli, D.R.. Current Practice of Clinical Electroencephalography. 4th Edition. Philadelphia: Wolters Kluwer, 2014

Question 220: Physiology - Basic Physiology

Discussion:

Gamma-Aminobutyric acid (GABA) and galanin-containing cells in the ventrolateral preoptic (VLPO) area and GABA cells in the parafacial zone (PZ) of the brainstem function to promote non-REM sleep. Hypocretin neurons are day-phase active. Monoaminergic neuronal systems arising in the brainstem and projecting to widespread cortical neurons are inhibited during REM sleep. Melatonin is a commonly used over-the-counter sleep aid, but this drug may not exert direct influence on the sleep-wake circuitry. Instead, melatonin is a marker of, and is strongly aligned to, the circadian timing system.

References:

Richard L. Horner, PhD ; John H. Peever, PhD. Brain Circuitry Controlling Sleep and Wakefulness. Continuum: Sleep Neurology p. 955-972 August 2017, Vol.23, No.4

Question 221: Physiology - EEG

Discussion:

Lateral eye movements are seen on the bipolar montages which are out-of-phase in derivations involving F7 and F8 electrodes as an increase in positivity at one is associated with a decrease in positivity in the other. Muscle activity produces very brief potentials. Movement of the tongue, whose tip is electrically negative with respect to its base, may produce widely distributed, low frequency intermittent potentials that may resemble "projected rhythms". A burst of muscle potentials may precede such low frequency waves, serving to differentiate glossokinetic potentials from "projected" activity. Rhythmic delta activity confined to a single electrode position likely represents pulse artifact. Sequential eye blink artifacts are identifiable by their location at Fp1, Fp2, their considerably lower amplitude at F3, F4 and their response to eye opening. Eye movement is the most common cause of physiological artifact in EEG recordings.

References:

Ebersole, J.S., Husain A.M., Nordli, D.R.. Current Practice of Clinical Electroencephalography. 4th Edition. Philadelphia: Wolters Kluwer, 2014

Question 229: Physiology - EMG

Discussion:

Nerve conduction studies with temporal dispersion, conduction block, and slow conduction are seen in chronic inflammatory demyelinating polyneuropathy. In hereditary motor and sensory neuropathy (Charcot-Marie-Tooth disease), there are slow latencies and nerve conduction velocities, but no temporal dispersion or block. In amyotrophic lateral sclerosis, nerve conduction studies may be normal or with decreased compound muscle action potential amplitudes. Nerve conduction studies are normal in facioscapulohumeral dystrophy and myasthenia gravis.

References:

Lewis RA. Chronic inflammatory demyelinating polyneuropathy. Curr Opin Neurol. 2017;30:508-512.

Question 252: Physiology - EEG

Discussion:

Nonconvulsive status can present with altered consciousness or cognition. It can develop in patients with seizure disorder, occasionally in elderly patients without a previous history of seizures, after antiepileptic drug or sedative medication withdrawal.

EEG findings in Creutzfeldt-Jakob disease would be repetitive, generalized 1 Hz sharp waves. Hepatic coma presents with triphasic waves on EEG. Generalized beta activity is seen with benzodiazepine toxicity. Alzheimer disease in early stages has normal EEG or mild slowing of background activity.

References:

Hocker SE. Status epilepticus. Continuum 2015; 21:1362-83

Question 260: Physiology - EEG

Discussion:

The EEG reveals right anterior temporal sharp waves with a maximum potential at T4-T2.

References:

Christopher T Skidmore. Adult Focal Epilepsies. Continuum 2016;22(1):94-115.

Question 264: Physiology - EEG

Discussion:

The major finding in the EEG is hemispheric asymmetry. In the absence of a skull defect, the side of the lower alpha activity is usually the abnormal one. In this case the left hemispheric attenuation is due to a large left hemispheric subdural hematoma. Alpha coma and hepatic encephalopathy both produce bilateral EEG abnormalities. Right-sided MCA stroke might be expected to produce focal slowing in the affected distribution. There is no evidence of ongoing epileptiform activity to support a diagnosis of status epilepticus. Finally, the clinical history of trauma makes subdural hematoma the most probable cause of the EEG asymmetry.

References:

Daube JR, editor. Clinical neurophysiology. New York: Oxford University Press, 2009.

Question 267: Physiology - EEG

Discussion:

The potential at point A is subtracted from the potential of point B which is -90V and by convention when point A is more negative than point B the deflection will move upward.

References:

Schomer D and Lopez de Silva F. Niedermeyer's Electroencephalography: Basic Principles, Clinical Applications, and Related Fields. Philadelphia, PA, Lippincott Williams & Wilkins, 2018

Question 269: Physiology - EEG

Discussion:

The presence of periodic lateralized sharp wave discharges in a patient with a recent febrile illness and onset of seizures would strongly suggest herpes simplex encephalitis. Clinical trials from the 1980s have demonstrates that administration of IV acyclovir leads to reduction of mortality from 70% to 30%. Acyclovir is currently the only FDA approved treatment for HSV encephalitis. Complications from this medication includes nephrotoxicity.

References:

Gnann JW, Whitley RJ.. Herpes Simplex Encephalitis: An Update. Curr Infect Dis Rep. 2017;19(3):13

Schomer D and Lopez de Silva F. Niedermeyer's Electroencephalography: Basic Principles, Clinical Applications, and Related Fields. Philadelphia, PA, Lippincott Williams & Wilkins, 2018

Question 278: Physiology - EEG

Discussion:

The patient has juvenile myoclonic epilepsy that is characterized by generalized tonic clonic seizures, absence seizures and myoclonic jerks. EEG demonstrates 4-6Hz spike wave discharges, polyspikes and a normal background.

References:

Wirrell E. Infantile, childhood and adolescent epilepsies. Continuum 2016; 22:60-93

Question 288: Physiology - EEG

Discussion:

Breach rhythm is seen on EEG with a skull defect. It appears as accentuation or increased amplitude of rhythms, especially theta, alpha, and beta, underlying the breach in the skull. Eye blinks can be seen as a surface positive downward deflection seen most prominently in the anterior derivations. Sleep spindles are sinusoidal activity best seen over the central regions at a frequency of 11 to 16 Hz. Mu rhythm has a sharp negative and a rounded positive phase seen best over the central regions at a frequency around 8-11Hz. Positive occipital sharp transients of sleep (POSTS) are seen as a sharp positive discharge maximal in the occipital regions.

References:

Schomer D and Lopez de Silva F. Niedermeyer's Electroencephalography: Basic Principles, Clinical Applications, and Related Fields. Philadelphia, PA, Lippincott Williams & Wilkins, 2018

Question 298: Physiology - Autonomic Studies

Discussion:

Heart rate changes in response to deep breathing depend on the presence of normal vagal innervation of heart.

References:

Low PA, Benarroch EE. Clinical autonomic disorders. 3rd ed. Baltimore: Lippincott-Raven, 2008.

Question 305: Physiology - EMG

Discussion:

Autoimmune myasthenia gravis is caused by IgG directed attack on the neuromuscular junction (NMJ). Although the amount of acetyl choline (ACH) released is normal, there is reduced binding of ACH to the ACH receptor, resulting in smaller end plate potential and defective neuromuscular transmission. LEMS involves the production of IgG antibodies directed at the presynaptic voltage-gated calcium channel. Congenital myasthenic syndromes have presynaptic defects of ACH packaging and release, deficiency of endplate acetylcholinesterase, and postsynaptic defects of the ion channel or the number of ACH receptors.

References:

Preston & Shapiro. Electromyography and Neuromuscular Disorders: Clinical-Electrophysiologic Correlations. 3rd edition, Elsevier Saunders, 2013

Question 313: Physiology - Sleep

Discussion:

The combination of a history of cataplexy with a short mean latency on a multiple sleep latency test (MSLT) is sufficient to make a diagnosis of narcolepsy, even in the absence of sleep-onset REM on an MSLT. Excessive daytime sleepiness (EDS) is often the first manifestation, with development of cataplexy months to years after the onset of EDS. Cataplexy may present up to one year before the onset of Sleep-onset REM periods (SOREM) on MSLT.

References:

Silber MH. Diagnostic approach and investigation in sleep medicine. Continuum 2017; 23: 973-988

Question 315: Physiology - EEG

Discussion:

Hypsarrhythmia is the most common EEG pattern seen in children with infantile spasms. The pattern is characterized by high-voltage diffuse slowing with multifocal spikes and sharps in a chaotic fashion.

References:

Pedley TA, Mendiratta A, Walczak TS. Seizures and epilepsy. In: Ebersole JS, Pedley TA, editors. Current practice of clinical electroencephalography. 3rd ed. Philadelphia: Lippincott, Williams & Wilkins, 2003.

Question 326: Physiology - EEG

Discussion:

Alpha (8-11Hz) patterns can be seen in comatose patients and in 3 different types of conditions. In anoxic encephalopathy usually secondary to cardio respiratory arrest alpha patterns are diffusely seen with a frontal predominance. In toxic encephalopathies this pattern is superimposed with beta frequencies. In locked-in states the alpha pattern is posteriorly dominant, reactive to sensory input and photic driving may be seen. Prognosis is poor for alpha coma states.

References:

Husain AM. Electroencephalographic assessment of coma. J Clinical Neurophys 2006; 23: 208-20.

Question 340: Physiology - EMG

Discussion:

The involvement of the femoral innervated muscles with sparing of obturator innervated muscles points to a femoral mononeuropathy as the most likely diagnosis. With the patient's history of anticoagulant use, an iliacus hematoma is a clinical consideration and could cause compression of the femoral nerve.

References:

Preston & Shapiro. Electromyography and Neuromuscular Disorders: Clinical-Electrophysiologic Correlations. 3rd edition, Elsevier Saunders, 2013

Question 356: Physiology - EMG

Discussion:

The description of acutely evolving symmetric weakness with hypoactive reflexes in a 45-year-old man should suggest the diagnosis of acute inflammatory demyelinating polyneuropathy (AIDP) or Guillain-Barre syndrome. Extremity pain may be a presenting feature. Nerve conduction studies are the best tests to perform in this case since they will demonstrate the electrophysiologic signatures of segmental demyelination in the form of motor conduction block and abnormal temporal dispersion of compound muscle action potentials. Early in the course of the disease, prolonged or absent F-wave responses may be the only abnormalities indicating proximal conduction block or delay. Needle EMG of affected muscles in this case will likely demonstrate reduced recruitment only at 1 week. Most of the other choices (fibrillation potentials, polyphasic motor unit potentials, and unstable motor units) indicate axonal loss or reinnervation. Complex repetitive discharges (CRDs) may be seen in either primary nerve or muscle disease and are usually observed in chronic processes.

References:

Preston & Shapiro. Electromyography and Neuromuscular Disorders: Clinical-Electrophysiologic Correlations. 3rd edition, Elsevier Saunders, 2013

Question 357: Physiology - EMG

Discussion:

In the Lambert-Eaton myasthenic syndrome (LEMS), single stimuli typically elicit a strikingly small compound muscle action potential. The amplitude varies over a wide range among different subjects. Thus, a decrease by as much as 50 percent of the maximal response in some individuals may still remain above the lower limit of a population norm. An apparent lack of reduction in amplitude, therefore, does not necessarily rule out the syndrome. A marked increase in CMAP amplitude (typically greater than 100%) follows 10 seconds of intense isometric exercise. The clinical features of LEMS include proximal muscle weakness (often more significant in the lower extremities) with decreased deep tendon reflexes. Autonomic symptoms and paresthesias may be seen as well. Bulbar symptoms are typically not prominent.

References:

Preston DC, Shapiro BE. Electromyography and neuromuscular disorders: clinical-electrophysiologic correlations. 3nd ed. Philadelphia: Elsevier, 2012.

Michael W. Nicolle, MD. Myasthenia Gravis and Lambert-Eaton Myasthenic Syndrome. Continuum: Muscle and Neuromuscular Junction Disorders p. 1978-2005 December 2016, Vol.22, No.6

Question 374: Physiology - EMG

Discussion:

The right femoral nerve innervates quadriceps muscle and mediates the sensory and motor portions of the knee reflex. The obturator nerve shows axonal injury. The site of lesion for involvement of both these nerves is most likely from a lesion in the lumbar plexus. The normal EMG of the paraspinal muscles argues against radiculopathy.

References:

Daube JR, editor. Clinical neurophysiology. New York: Oxford University Press, 2009.

Question 399: Physiology - EEG

Discussion:

Creutzfeldt-Jakob disease (CJD) is a prion disease that causes rapidly progressive dementia, myoclonus, and periodic, short-interval (0.5 to 1.0 second), generalized, bisynchronous triphasic sharp wave discharges on EEG. Periodic sharp wave complexes have a positive predictive value of 95% for CJD and occur in over two thirds of sporadic CJD patients during their disease. Herpes simplex encephalitis would be consistent with focal periodic discharges while hepatic encephalopathy would have triphasic wave, but the clinical presentation would be that of a waxing and waning encephalopathy. Subacute sclerosing panencephalitis has an EEG consistent with high amplitude repetitive sharp-slow wave complexes with high amplitudes recurring between 4-15 seconds and not at 1 second intervals.

References:

Malek N, Baker MR, Mann C, Greene J.. Electroencephalographic markers in dementia.. Acta Neurol Scand. 2017;135:388-393.

Markand ON and Brenner RP. Organic brain syndromes and dementias. Organic Brain syndromes and dementias. In: Ebersole JS and Pedley TA. Current Practice of clinical electroencephalography. Philadelphia: Lipincott Williams and Wilkins, 2003: 378-494.